

# California

## MEDICINE

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**PROTECTION**

**PROTECTION** against congenital syphilis can often be accomplished by treatment of the expectant mother.

# California M E D I C I N E

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## Anesthesia For Emergency Surgical Procedures\*

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**E**MERGENCY surgical procedures are frequently necessary when shock is present due to trauma, hemorrhage or to rupture of a viscus. In each instance the general clinical condition of the patient must be carefully considered when the type of anesthetic to be given is being decided upon.

Every surgeon recognizes the fact that adequate exposure, hemostasis and gentleness in handling tissues are essential. The anesthetist can aid in securing these factors by producing adequate muscular relaxation. When this can be secured without undue disturbance of normal physiologic functions, the patient's chances for survival are increased.

Before an anesthetic agent is selected its pharmacologic action should be considered and this action correlated with the clinical condition of the patient. It is generally accepted that ether produces a general peripheral vasodilation and when carried to the lower planes, a depression of vasomotion is common. Pentothal sodium also produces a peripheral vasodilation. Spinal anesthesia and regional blocks produce vasodilation in the anesthetized area. Frequently there is a compensatory vasoconstriction in the un-anesthetized area.

The body's first reaction to blood loss or trauma preceding shock is a peripheral vasoconstriction. This is the automatic attempt of the body to maintain sufficient blood for the vital centers. Following the administration of blood or plasma to patients who have had a severe drop in blood pressure, the pressure may rise to 100 or 120 systolic. This rise may occur before the total volume of blood lost has been replaced and is only possible because of the peripheral vasoconstriction still present. The administration of an anesthetic which

produces vasodilation at this time will produce an immediate severe drop in blood pressure.

Before any type of anesthetic is administered the patient should have:

1. Treatment of shock by administration of whole blood in adequate amounts.
2. Adequate premedication to allay pain and apprehension.
3. The stomach emptied, if food has been taken shortly before or following injury.

Sound surgical practice requires that normal physiology be maintained during operations and following. Patients suffering from trauma or hemorrhage or in shock from any cause prior to surgery, should have adequate treatment before any anesthetic is administered. The fundamental physiological abnormality in shock is an imbalance between the volume of circulating blood and the vascular bed. This may be due to loss of blood, loss of fluid, or to peripheral vasodilation.

Knowledge of the hemoglobin, hematocrit volumes per cent and plasma protein content of the blood will aid in determining the type of fluid most indicated.

	Hemoglobin	Hematocrit Vols Per Cent	Plasma Protein Grams Per Cent
Normals: .....	13.5-15.0	42-47	6.3-7.5
Shock Traumatic without Hemorrhage .....	15.0 and over	45-60	7.6-9.9
Dehydration with Shock .....	15.0-20.0	50-60	7.6-9.9
Burns (Severe) ....	20.0-21.0	60-70	4.1-5.
Hemorrhage (Severe) .....	7.0 or less	28 or less	5.8-5.1
Shock—Traumatic with Hemorrhage ..	10 or less	35 or less	6.5-5.5

There is no substitute for whole blood. Plasma restores the blood pressure and provides protein, but only whole blood contains the erythrocytes essential for the transport of oxygen. The amount

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of whole blood needed is the amount required to restore and maintain normal physiology.

#### RH FACTOR

Eighty-five per cent of the white race and 94 per cent of negroes have red blood cells containing Rh agglutinogens, and these individuals are called Rh Positive. Rh positive recipients are never susceptible to Rh incompatibility reactions.

Rh negative recipients lack Rh agglutinogens. They will never react unfavorably to Rh negative donors, nor to the first Rh positive donor, or to a series of Rh positive donors if the transfusions are given over a short period of time. They may become iso-immunized to transfusions of Rh positive blood so that a subsequent transfusion with Rh positive blood leads to an incompatible reaction. The limits of the danger and safety zone are not definitely known. At present it is thought that if an Rh negative recipient has received a transfusion of Rh positive blood ten days or more before receiving the second transfusion from an Rh positive donor, an incompatibility reaction may result. From the practical point of view, if a patient is receiving repeated transfusions and the interval between the first and last is ten days or longer, some danger exists. The first reaction due to Rh incompatibility is rarely severe in the male. If a reaction occurs in these circumstances in a patient who has not been tested with Rh grouping serum, no further transfusions should be given until he has been tested. If he be Rh positive, the reaction must have been due to something other than Rh incompatibility. If he be Rh negative, all subsequent transfusions should be from Rh negative donors.

The symptoms of hemolytic transfusion reactions consist of:

1. A sense of increased heat in the skin.
2. Headache.
3. Sense of constriction in the chest.
4. Pain in the lumbar region.
5. Rigor.
6. Fever.

The first 100 cc. of every transfusion should be given slowly and if any of the above symptoms appear, the transfusion should be stopped at once.

The dangers of giving excessive quantities of fluids is about equivalent to that of giving too little. Pulmonary edema may result from pushing too far the administration of fluids. Patients with reduced pulmonary circulation due to collections of pleural air, fluid or blood, require careful and repeated observation of the condition of the circulation, and all fluids should be administered with caution.

When it is impossible to control hemorrhage and surgical intervention becomes necessary in the presence of shock, two or more large needles should be inserted and an adequate supply of blood should be available before starting the anesthetic. In this way blood can be administered rapidly until the bleeding point can be found and the hemorrhage checked. Frequently 3,500 cc. or more of blood may be needed rapidly.

Clinical experience has demonstrated that pa-

tients in shock do not tolerate spinal anesthesia well. Likewise they do not do well under deep ether anesthesia nor pentothal. These contraindications are relative and depend to a certain extent upon the care that is given the patient by the anesthetist. For instance, a patient in shock due to injury to the lower extremity may do well under spinal anesthesia if the dose is small and the height of anesthesia restricted to the lower extremities. Likewise, pentothal can be used for a patient in shock, if adequate oxygen is given and the dosage kept to a minimum far below that required for a patient in good condition.

In most cases where muscular relaxation is essential, some type of regional block offers the patient the greatest margin of safety. By relieving pain, it is of definite benefit in preventing the onset of shock. Thoracic injuries where breathing is decreased because of pain show marked improvement following intercostal block.<sup>1</sup>

The use of regional field block for head injuries, brachial block for upper extremities, paravertebral block for reduction of dislocations of the vertebrae, intercostal or abdominal field block for abdominal surgery, has been described repeatedly in the literature and in textbooks. When the anesthesia produced by a block is not adequate, it should be supplemented with a general anesthetic. For patients in shock or impending shock, cyclopropane is the agent of choice as it disturbs the normal physiological processes less than any of the other agents.

Of the local anesthetic agents available, three are used most often—Procaine, Intracaine and Metycaine. Procaine is the least toxic of these agents and Intracaine is slightly more toxic. Using cocaine as a basis of comparison with an intravenous toxicity of one, Procaine is one-quarter as toxic, Intracaine is one-third as toxic and Metycaine three-quarters as toxic. Since all untoward reactions to local anesthetic agents are due either to rapid absorption into the blood stream or to an intravenous injection, the intravenous toxicity is the only one to be considered. An overdose of any of these agents produces respiratory paralysis ahead of cardiac failure, so there is usually adequate time for resuscitative measures.

The duration of anesthesia obtained in regional blocks will vary with the accuracy of the block and the amount of solution deposited in close proximity to the nerve. Procaine ordinarily produces anesthesia for 90 minutes, Metycaine lasts longer than Procaine, and Intracaine lasts 180 minutes. Intracaine and Metycaine have no antagonistic action to the sulfa drugs.

My associates and I have now used Intracaine for all types of regional blocks in well over 2,500 cases. The onset of anesthesia has been rapid and the number of untoward reactions has been minimal. Because of the rapid onset of anesthesia and the duration, we consider it the agent of choice.

#### SUMMARY

In emergency surgical procedures where shock is a factor, regional block alone or supplemented



with cyclopropane offers the patient the greatest margin of safety.

Replacement of fluid loss before administration of any anesthetic is desirable. When this is not feasible, adequate amounts of whole blood should be available for use during and following the operation.

An anesthetic agent and method should be used

that will not further accentuate the degree of shock present.

305 South Westlake Avenue.

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## Treatment of Bladder Tumors\*

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IN the compilation of this paper an effort has been made to evaluate the results of different modes of treatment of vesical neoplasms. The use of radiation in the form of radon emanation seed implantation is given special study.

There have been numerous reports of the use of radiation in the treatment of bladder tumors, but the results have been so varied that it is difficult to draw a definite conclusion as to the efficacy of this therapy. Beer<sup>2</sup> in his monograph on the subject reported that the use of radium is unsatisfactory, and that radical surgery is preferred. Barringer<sup>1</sup> in 1934 stated that the implantation of radon seeds was the ideal treatment for vesical neoplasms, but Dean and Balfour<sup>3</sup> in 1941 were not enthusiastic about the results of any treatment. However, in their series, 14 per cent of 52 cases of infiltrating carcinoma lived more than five years after radiation. Parmenter<sup>4</sup> found that patients treated with resection and fulguration, followed by implantation of radon seeds or application of radium, progressed more satisfactorily than those who did not obtain this treatment.

Endoscopic electrosection and fulguration has been the method used for removal of the tumor in most of the cases reported here. When this is performed properly, it is preferable to suprapubic removal, unless the tumor is more than five centimeters in diameter, or unless it is situated in the ventral portion of the dome of the bladder. A more thorough removal of tumor tissue can be accomplished through the endoscopic approach because the tissue can be examined minutely and thoroughly through the lens system of the instrument, and a differentiation between tumor tissue and bladder muscle tissue can be made.

From this observation it can be determined whether all the tumor tissue has been removed. Some tumors infiltrate beyond the bladder wall, and in these cases removal by any method is incomplete. There is danger in resecting entirely through the bladder wall, and an extravasation into perivesical tissues resulting when the endoscopic approach is used; but this is minimized

when the operator is familiar with the difference in appearance of the tissues. When the bladder musculature is seen through the lens, no more tissue is removed from that particular area. Elongated bundles or strands of tissue of varying thicknesses, which have a glistening, somewhat fibrous appearance, are characteristic of bladder muscle, whereas tumor tissue is granular or fuzzy and is of a softer and more homogenous texture. When the removal of tissue extends through the bladder wall, a darker or black area, crossed by numerous spider weblike strands, appears. If this is immediately recognized, and the resection discontinued, suprapubic drainage of the bladder or of the perivesical spaces is not necessary. When, on the other hand, it is not recognized, and distention of the bladder is continued until there is extravasation of considerable fluid, perivesical drainage through a small suprapubic incision is indicated, but cystotomy is seldom necessary. Tumors more than five centimeters in diameter, and those situated in the ventral portion of the bladder, should be removed through the open approach.

#### SOURCES OF DATA

The data presented in this paper was derived from a review of 537 cases of bladder tumor obtained from our office files which were seen between the years 1926 and 1945. Of these, 186 cases were eliminated from the study because of insufficient data. Inability to obtain recent follow-up reports was the chief reason for their rejection, and many were not included because of lack of grading of the tumor as to malignancy. There remained a total of 349 cases which were used. Inasmuch as there were so few which had open surgery, in comparison with those having endoscopic electrosection, and inasmuch as the results of treatment in these two groups were very similar, a further breakdown into the different methods of approach in removing the tumor would be somewhat confusing and of very little significance.

The term electrosection and fulguration, as used here, signifies the removal of the major portion of the tumor with the cutting current and loop electrode, either endoscopically or through a-suprapubic cystotomy opening, and fulguration

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of the base and edges of the resected area with the dessicating current. In this study, the above mode of treatment, without the subsequent implantation of radon emanation seeds, is compared with the same treatment plus the implantation of radon.

The size of the tumor influenced the length of life of the patient. Inasmuch, however, as the average size in the two groups of patients studied (those with radon treatment and those without) were similar, this factor made no significant difference between these two groups.

During the past five years radiation has been used in the form of radon emanation seeds implanted into the tumor-bearing area in most cases having a grade II or more malignancy. The papillomata and grade I malignancies, which have been grouped together in this report, were seldom treated with radiation because the tendency in these cases is for the recurrence of the tumor to be in a different location in the bladder from the original growth. Therefore, the implantation of radon seeds into the site of the original tumor would be of no value. The usual time of implantation of the seeds was four weeks following resection and fulguration of the growth. By this time most of the dessicated tissue had sloughed away, and a deeper, more accurate implant was possible. Two and five tenths millicure seeds placed one centimeter apart were used during the first few years; but more recently, due to the fact that smaller seeds were more available, one and five tenths millicure seeds, placed about one-half centimeter apart throughout the tumor-bearing area of the bladder wall, and embedded about one centimeter deep, have been used. In most cases the implantation was done through the cystoscope, and if this is performed correctly, it is as accurate as when the open suprapubic approach is used.

The compilation of the statistical data separates the living patients from those who have died, for in so doing a more accurate evaluation of the results can be obtained. For example, if these were all considered together, a patient with a papilloma who was followed for two years and was still living would be counted as having the same survival period as a grade II carcinoma who died in two years. This would obviously be an erroneous comparison.

The most accurate comparison of results of treatment can be obtained from Table I, for all of these cases were followed until death, thus eliminating the indeterminate factor of the future life expectancy in the group who are still living. The data in this table shows that patients with grade II and III tumors who were treated with electrosection plus implantation of radon emanation seeds, lived longer than those in the group which did not receive the radiation. This difference is significant for the average length of life from the onset of symptoms to death in the group who had no radon seeds implanted was approximately two-thirds of that in the group which received the radiation. None of the patients who had papillomata or

grade I malignancies treated with radon seeds are dead.

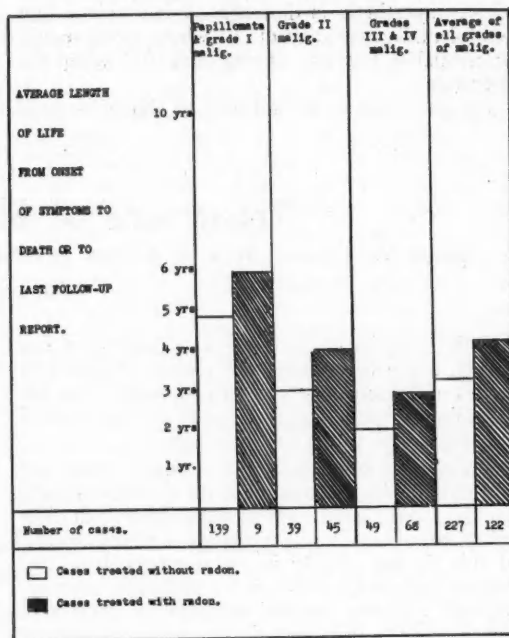


Table 1.—Group of patients with bladder tumors who have died. Comparison of those treated by electrosection and fulguration alone with those treated by these modalities plus implantation of radon emanation seeds.

Table II gives the length of life from onset of symptoms to the last follow-up report in the patients who are still living, and compares the group which had implantation of radon seeds with the one which did not have the radiation. There is a significant increased length of life in the former group. Similar results are obtained when combining the group who are dead and those who are still living as shown in Table III. All of these patients had electrosection and fulguration of the tumor.

Table IV gives the present status of all cases treated, showing a comparison between those treated by electrosection and fulguration only with those treated by these modalities plus implantation of radon emanation seeds. The percentages given show a comparison between the radon treated cases and the non-radon treated cases. They indicate the proportion of cases in each malignancy grade group treated without radon who are dead, who are still under treatment or arrested less than one year, who are arrested for one to five years, or who are arrested over five years, in comparison with the cases in the same malignancy grade group treated with radon who are dead, arrested less than one year, arrested for one to five years, or arrested over five years. The group of those who are arrested for less than one year is composed of those patients who are still under treatment and upon whom repeated resections, fulgurations, and/or implantation of

radon seeds are being done at less than yearly intervals.

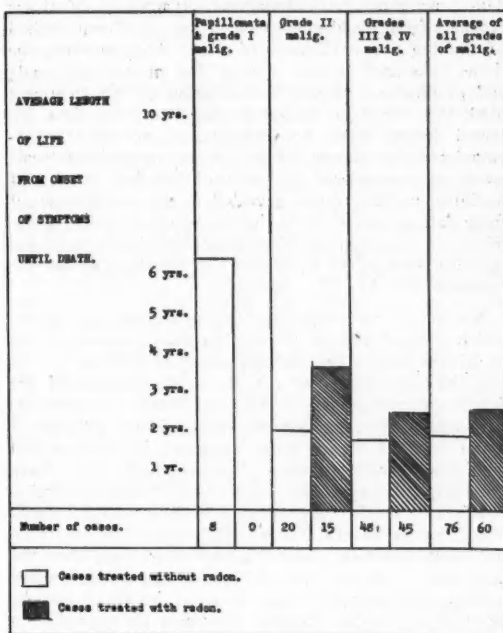


Table 2.—Group of patients with bladder tumors who are still living. Comparison of those treated by electrosection and fulguration alone with those treated by these modalities plus implantation of radon emanation seeds.

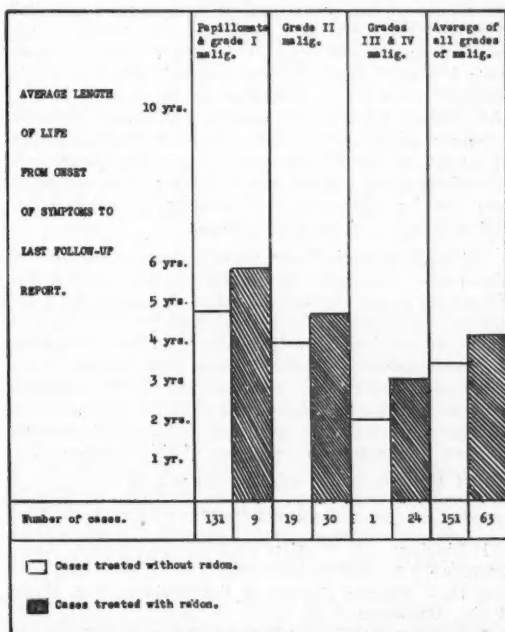


Table 3.—Group of patients with bladder tumors (living and dead) followed more than one year. Comparison of those treated by electrosection alone with those treated by these modalities plus implantation of radon emanation seeds.

Inasmuch as the majority of patients treated with radiation in this series have been seen during the past five years, there are not many who are listed as arrested more than five years. However, the table does show a definite tendency toward a larger number being arrested one to five years in the group treated with radiation.

Grade of Malignancy.	No. of Pts.	Without or With Radon Seeds		No. of Pts.		Pts. Dead		Under Treat-ment		Arrested over 5 yrs.		Arrested over 5 yrs.		
		No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	
Papilloma and grade I malig.	148	Without Radon		139	8	6	39	26	72	48	20	14		
		With Radon		9	0	-	4	3	5	3	0	-		
Grade II malig.	64	Without Radon		39	20	24	10	12	8	10	1	1		
		With Radon		45	15	18	14	15	18	1	1			
Grades III & IV malig.	117	Without Radon		49	48	41	0	-	0	-	1	1		
		With Radon		68	45	39	19	15	4	3	1	1		
All Grades	349	Without Radon		227	76	22	49	14	60	22	22	7		
		With Radon		122	60	17	37	10	24	7	2	1		

\* Indicates the percent of all patients treated without radon in each grade of malignancy who are dead, under treatment, arrested etc. In comparison with all patients treated with radon in each grade of malignancy who are dead, under treatment, arrested etc.

Table 4.—Comparison of results of treatment of bladder tumors by electrosection and fulguration alone with those of treatment by these modalities plus implantation of radon emanation seeds.

It is evident from this study that the more malignant the tumor is, as determined by histopathological examination, the shorter is the life expectancy of the patient. All the tables show that the patients with a papilloma or grade I carcinoma live longer than those having a grade II malignancy, and these in turn outlive the ones with a grade III or IV neoplasm. It can, therefore, be definitely stated that the grading of a bladder tumor aids the surgeon in giving a prognosis to his patient.

#### SUMMARY AND CONCLUSION

In this series of 349 cases with bladder tumor, there is a significant difference in results of treatment between the group which received electrosection and fulguration without radon emanation seeds, and the group which received this mode of treatment plus radon. The latter group have a longer life expectancy, and the results of treatment are superior to those obtained in the first group.

The study also shows that the higher the grade of malignancy of the bladder tumor, the poorer the prognosis, and that in general the results of the use of radon seeds in the more malignant tumors (grades III and IV) are not as good as when used in the grade II tumors.

DISCUSSION BY H. C. BUMPUS, JR., M.D., PASADENA

Contributions such as this excellent survey by Dr. Barnes and his associates dealing, as it does, with a comparison of the results obtained in treating tumors of the bladder by two different methods seems to me absolutely essential if urologists are ever to reach an agreement as to the best method of treating these unfortunate patients.

At a recent meeting of the Western Branch of the American Urological Association this subject was being discussed and one of the members recalled that a decade ago he had asked the guest speaker, Dr. N. G. Alcock, how he was treating tumors of the bladder. Dr. Alcock replied, "The surgeons have had a go at it; I'm using radiation in the future—the results cannot be worse." Now, after a lapse of ten years, Dr. Alcock told the members that while the results hadn't been any worse, he didn't believe they had been any better. He was now in favor of radical surgery, believing that the improvement in technic and chemotherapy during the past ten years would result in sufficient cures to warrant the increased risk. He remarked, "After all, it is a cure that we are shooting at!"

It happens that the method Dr. Barnes uses, of electrosection and implantation of radon seeds, is the one I have usually employed. Perhaps that is why I was asked to discuss this paper. The dictum of "kill or cure" so frequently followed in cases of malignancy has never had much appeal for me. It so completely disregards those cases that are neither killed or cured. These unfortunates are too frequently doomed, not alone to periods of post-operative discomfort, pain and suffering, but frequently succumb to their malignancy far sooner than if no attempt had been made to cure them. Were it, in fact, a choice between death and cure, I could agree, but cures have occurred too infrequently to offset the high mortality and morbidity incident to such efforts.

Electroexcision with radon implantation, on the other hand, the results of which Dr. Barnes has so carefully studied, carries neither the mortality rate nor the morbidity associated with more radical methods. Yet it offers for a greater number of any group a prolongation of life and occasionally a possible cure. That, on the whole, adds up, I believe, to more years of life than the occasional cure by radical surgery.

I hope, as Dr. Alcock does, that in the future a report as convincing as Dr. Barnes', showing beyond question that surgery is as superior to electro-coagulation and radon implantation as Dr. Barnes has shown radon implantation is superior to electro-excision alone, will be published: to date none exists.

#### DISCUSSION BY GILBERT J. THOMAS, M.D.

Dr. Barnes has given us in his paper an evaluation of results of the methods of treatment of urinary tumors employed by him, with special references to the use of radiation in the form of radon emanations. The writer uses endoscopic electrosection and fulguration which his experience indicates is preferable to suprapubic removal unless the tumor is more than five centimeters in diameter or situated in the ventral portion of the dome of the urinary bladder.

The result of treatment of urinary bladder tumors of all grades are very disturbing to me and to most urologists. We have changed our methods of treatment when new weapons were developed such as resection, fulguration, X-radiation, and radon seeds. Combinations of these methods of treatment have been employed and yet the cures are few; the recurrences continue and patients' survivals are not lengthened very much when all urologists' results are tabulated and their methods of treatment are evaluated. In other words, we are not gaining control of bladder tumors, and we produce few cures. Why is this so?

Dr. Barnes has just suggested a combination of weapons that he used to control bladder cancer that has produced the best results, i.e., comfort to the patient and longer survival, but not cures.

For a number of years the American Urological Association

has maintained a bladder tumor registry at the Army Pathological Museum in Washington, D.C. This registry was created because we want to centralize all data concerning the pathological examination of tissue obtained from bladder tumors and use a uniform method of grading the malignancy of these. Accompanying the tissue submitted to the registry for microscopic study and grading, we require a description of the treatment used, the immediate results produced and the data obtained during follow-up examinations, so that the accumulated data should reflect the best methods of treatment to be employed for each of the four grades of malignancy. The results revealed in the compilation of these data as published by the Carcinoma Registry Committee of the American Urological Association were and still are poor and no consensus has developed among the members.

My opinion concerning the treatment of bladder tumors which is based on over 30 years' experience in clinics and in private practice may be epitomized as follows:

1. We have failed to get a correct estimate of the degree of malignancy of bladder tumors, because we have not obtained specimens of tissue from that part of tumor in which we are most interested, i.e., its base and the bladder wall adjoining. Specimens of tissue from these important areas are rarely obtained transurethrally. If this method of biopsy is employed, injury to and sometimes rupture of the bladder wall may occur. If these statements are true (and I believe they are), then the diagnosis of the presence of malignant change in the tumors, and their gradation, in many instances may be incorrect. How can adequate treatment be applied if a wrong pathological diagnosis is obtained?

2. Why should cancer of the urinary bladder, which metastasizes early, be treated differently than other malignant growths? When cancer occurs in other anatomical areas, the slogan is early correct diagnosis of the nature of the tumor, and if malignant change has occurred, then early, wide and complete removal of the involved area or the organ. *Cystectomy partial or complete is now reserved for tumors that cannot be easily attacked through the urethra or are pronounced inoperable.* When the removal of adjacent organs becomes necessary this is not a different condition to that associated with cancers in other organs or tissues. Cancer is a life-taking disease at any age, and our aim should be to save lives by eradication of this disease and not be satisfied with any method of procrastination.

3. Complete surgical removal of cancer of the bladder aimed at a cure should be our method of attacking this life-taking disease. It should be done as soon as the diagnosis of malignancy is made. Complete surgical removal should be the first method of attack, and not used when the local condition is obviously inoperable, because of its extent, and destructive effect, or because the patient's general condition has been damaged by the toxemia from the cancer so that he or she cannot withstand the trauma incident to any surgical operation of this magnitude.

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## The Onset of Ovulation During the Puerperium\*

ROBERT A. LYON, M.D. AND MARY JANE STAMM, M.D., *San Francisco*

THE physiology of reproduction may be considered to pivot about the process of ovulation. This event ordinarily occurs in the young adult within two years after the onset of the first menstruation. It is the result of progressively increasing secretion of gonadotrophic hormone, sufficient in later cycles, to bring about the normal follicular maturation culminating in ovulation. In a similar way the factors influencing the ovaries following parturition until normal cycles recur are insufficiently known.

The intent of this presentation is to report an investigation† of the pattern and time of recurrence of ovulation following parturition, conducted primarily by means of the basal body temperature method.

Ovulation in non-lactating puerperae appears at an average time of 10.2 weeks post-partum.<sup>5</sup> Other workers, Griffith and McBride<sup>5</sup> utilized the endometrial biopsy method of studying various endometria, among them a series of 21 normal puerperal women observed for two to twenty-four weeks post-partum. They were divided into lactating and non-lactating groups. The former lactated over a range of two to nine months. Menstruation and ovulation occurred while lactation was still going on in as many as 20 per cent. The remainder had neither ovulation nor menstruation until after weaning. According to these observers, lactation continued three and five-tenths months with anovular flow at an average of five months, while the average of the initial ovulations appeared at five and five-tenths months. These observers noted further that the non-lactating patients menstruated at an average of two months post-partum and ovulated quite late, apparently not prior to five months post-partum. Moreover, ovulation was preceded by anovular menstruation in 95 per cent of these non-lactating women.

Kurzrok, Lass and Smelser<sup>3,4</sup> studied 30 lactating patients who were menstruating, and noted 55 per cent of this selection had anovular cycles. Accordingly, a high incidence of ovulatory cycles in lactating women who menstruate can be expected.

Topkins<sup>9</sup> also observed a small series of 28 puerperal women from whom he secured 45 biopsies over weekly intervals. He was interested in the degree of ovarian suppression during lactation as reflected in the endometrium. These en-

dometria were in a static phase in 85 per cent and suggested that the follicles neither regressed nor matured ordinarily during lactation. Proliferation was present in 94 per cent (136 specimens) of which 15 per cent were temporarily hypoplastic. Hence, but 6 per cent of the tissues were progestational.

Routine endometrial biopsies from presumably healthy young women show anovulation in approximately 5 per cent of all cycles.<sup>6</sup> Moreover, in patients with low fertility, Rock<sup>7</sup> observed that 9.1 per cent had anovular cycles. These data, together with Kurzrok's finding of about 40 per cent ovulatory cycles in menstruating, lactating puerperal women, are the available background for studies regarding normal ovarian function following parturition.

Studies of the early and late puerperium which show endometrial, basal temperature, ovulatory and progestation dissimilarity from the non-puerperal cyclic woman, may be a basis for a revision in our conception and terminology of the puerperium. While many arbitrarily use a six weeks limit for this term, in a physiological sense it may encompass a longer period, as the puerperal transition to the normal state seems to be gradual and extended.

The basal body temperature method of observation has been well described and the method seems to be established on a firm basis in the puerperal woman.<sup>8</sup> A sufficient number of endometrial biopsy correlations have established that in the normal progestational (raised temperature) phase there are regularly found definite secretory changes in the endometrium, which in turn are followed within a few days by menstruation.

### PROCEDURE

Fifty unselected puerperal women, aged 18 to 37, most of whom were primiparae, have been followed by means of the basal body temperature method for resumption of the normal ovarian cycle from the time they left the hospital until approximately six months post-partum. Basal body temperatures were taken per rectum at approximately the same time each morning before rising. Endometrial biopsies were taken in selected cases for correlation purposes during the phase of elevated basal temperatures, during the time that a functional corpus luteum would be expected.

### RESULTS

The patients observed in this study may be divided into three groups according to the duration of lactation. Twenty-four of them lactated for one week or less; seventeen continued for a month and nine lactated for one to three months.

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In the group of non-lactating patients, the average onset of the catamenia was 7.7 weeks post-partum, for those lactating a month the initial menstruation occurred at 7.9 weeks, while for the group lactating longer, namely from four to twelve weeks, the average menstruation occurred at eleven weeks post-partum. It appears that the average onset of menstruation is delayed following parturition in proportion to the length of the lactation period. The interval of lactation duration to the first menstruation (L-M) decreases progressively from 7.7 weeks to four weeks in those lactating for four weeks and to 1.7 weeks in the remaining group of those lactating for more than four weeks.

The initial ovulation following parturition in those cases which did not lactate occurred at an average of 10.2 weeks, increased slightly to 10.6 weeks when lactation continued for four weeks and appeared at an average of 17.0 weeks after three months of lactation. Thus, the lactation to ovulation (L-O) interval decreased markedly from ten weeks in the non-lactating group to 6.6 weeks in the four weeks lactation group and to 0.4 of a week in those lactating about two months. The L-O interval mean became zero by eight months post-partum.

The endometrial biopsy specimens show stromal growth with striking large spindle-like cells, abundant loose reticulum and notable hypovascularity. Many apparently resting endometria actually have distended uterine glands which appear to be stimulated mildly, often growing closely together. In sequence to the estrogenic manifestation, when ovulation has occurred the progestational effects ordinarily seem incomplete and quantitatively slight.

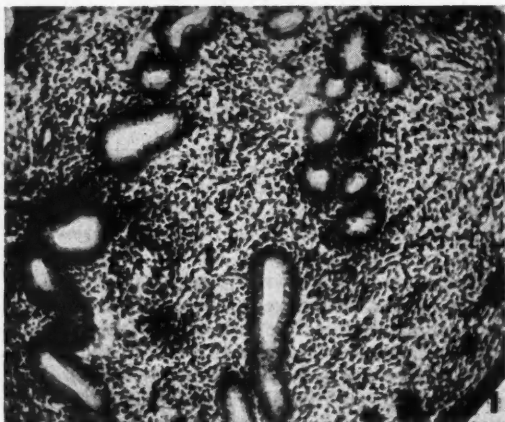


Fig. 1.—A. A. No lactation. Resting place (moderate estrin effect) at fifth week post-partum.

These observations suggest that frequently there occurs an incomplete progestation of markedly dilated glands which appears to be associated with a relatively short, low progestational basal temperature curve. Moreover, the frequent prolongation of menstruation is associated with either

this hyperplasia of proliferative endometria or incomplete progestation.

Figure 1 illustrates a resting phase correlated with relatively constant low basal temperatures. Figure 2 is from a patient who lactated four weeks and appears to have ovulated at eight and

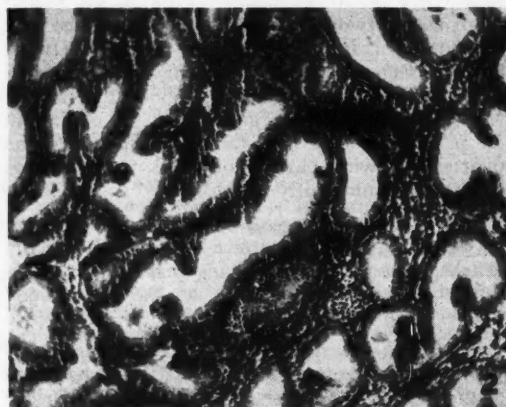


Fig. 2.—J. W. Lactated four weeks. Sixth day of progestational phase (22nd day of a 25-day cycle) at the 12th week post-partum.

twelve weeks post-partum. The endometrium was taken on the sixth day after the presumed ovulation and shows slight progestation of dilated glands. Figures 3 and 4 are from the same patient (D.S.) taken at eight and eleven weeks respectively. Progestation is slight but sufficient to confirm the basal temperature rise indication of ovulation.

Charts 1, 2, 3 and 4 illustrate ovulatory cycles following varying lengths of lactation. The cycle pattern, length of menstruation and time of ovulation are examples typifying the average patient's records.

The non-lactating puerperal cycle, which starts with menstruation at about eight weeks post-

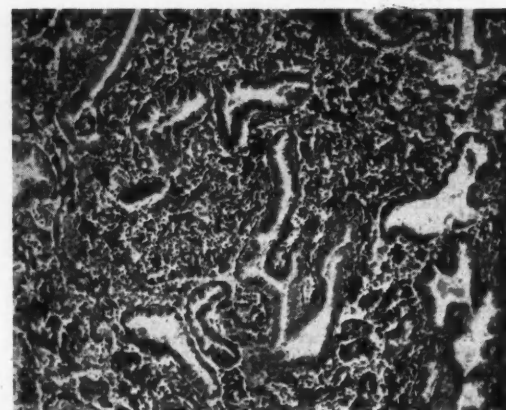


Fig. 3.—D. S. First day of menstruation at eighth post-partum week of a non-lactating woman. Deficient progestation and menstrual autolysis.

partum, has a characteristic tendency to be prolonged. When ovulation is first resumed, it tends to occur late in the cycle and the progestation phase seems shortened, with a greater tendency to menorrhagia than in normal cycles of the same individual. However, of the two changes, prolongation is usually more marked than the increase in the volume of flow.

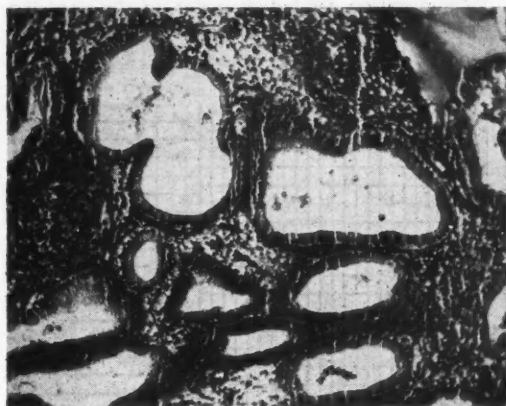


Fig. 4.—D. S. No lactation. Deficient progestation in same patient as Figure 3, taken on day 22 of a 24-day cycle at 11th week post-partum.

During subsequent cycles the corpora probably resume a quantitatively normal function as reflected by successively improved progestational endometrium, shorter cycles, earlier ovulation, less menorrhagia, increased basal metabolism, and longer progestational phases of the cycle.

Anovular menstruation, which constitutes the initial bleeding in about 95 per cent of the non-lactating group, tends to be more prolonged than after ovulation has appeared. There seems to be an inverse correlation between the length of the progestational phase and the average duration and intensity of uterine bleeding.

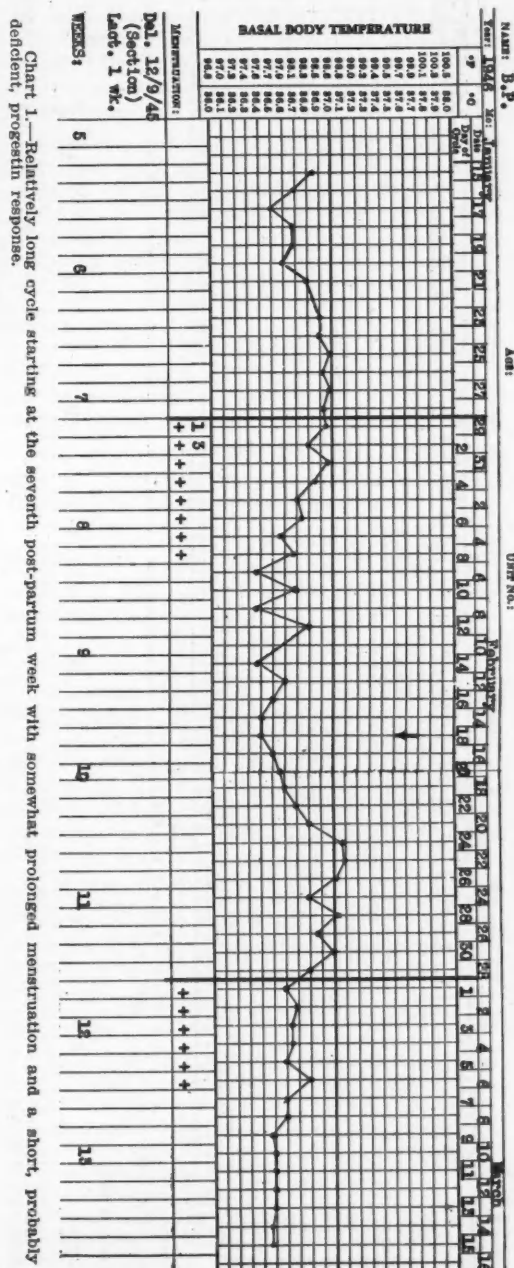
When menstruation occurred relatively early during the puerperium, especially in the non-lactating woman, the cycle tended to be irregular or prolonged and the menstruation which accompanied these cycles also tended to be more than six days' duration. The actual blood loss was not ordinarily great, despite the tendency to menorrhagia. This refers particularly to the anovular cycle. When ovulation occurred the cycles followed the characteristic pattern for that individual. When an ovulatory cycle was prolonged, the time of ovulation was ordinarily late in the cycle.

In general, the basal body temperatures were lower during the puerperium and continued so until about the time of the initial ovulation. This could derive from a puerperal lowering of the metabolism. Further points suggesting decreased metabolism were, the relatively low basal temperatures found during lactation, slowness of the pulse, sensitivity to cold, the readiness of fatig-

ability, low reserve of strength, and the relative promptness with which menstruation and ovulation recur when pregnancy or lactation is terminated at any stage. Moreover the fluctuation in basal temperature from day to day during the puerperium seemed to be more extensive than in the regularly ovulating cyclic woman.

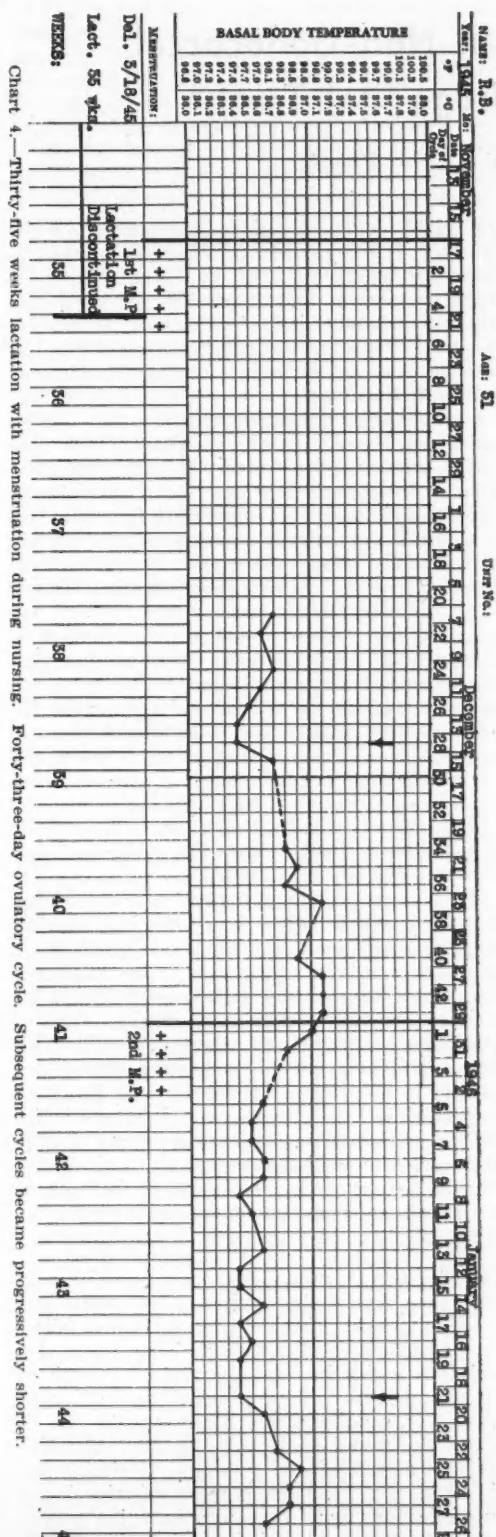
#### DISCUSSION

From the functional viewpoint, during the puerperium there is a gradual preparation of con-









of lactation after the third puerperal month, and conversely, prior to the third month post-partum, lactation almost always ended before menstruation occurred. Also, after prolonged (over three months) lactation, ovulation ordinarily precedes menstruation. However, the non-lactating and short-lactating patients regularly develop anovular menstruation prior to their initial puerperal ovulation.

Those who menstruate during lactation frequently also ovulate,<sup>4</sup> the conditions which cause the inhibition of the gonadotrophins being improved sufficiently to permit menstruation and subsequently, with less suppression, ovulation. On the other hand non-menstruating lactating women very rarely ovulate as in these, inhibition of the gonadotrophins is relatively complete.

While the nursing woman tended to have the first ovulation within a month of the cessation of lactation, it was deferred until about ten weeks post-partum in those not lactating. Thus the effect of recent pregnancy (apart from the effect of lactation) tended to inhibit the initial ovulation.

#### CONCLUSIONS

1. The puerperium is marked by temporary secondary ovarian failure which gradually improves, ordinarily culminating in the return of normal ovarian cycles.

2. Menstruation of the anovular type regularly precedes ovulation in the early puerperium, less frequently in the late puerperium.

3. The basal temperature method correlates satisfactorily with endometrial biopsies as a method of estimating ovulation in the puerperal woman.

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## The Use of Penicillin in Non-Gonococcal Infections of the Urogenital Tract\*

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SUCH brilliant clinical cures have attended the use of penicillin in the treatment of gonococcal infections that the early attention of urologists was directed chiefly to its application in these conditions. So long as the supplies of the drug were limited, it was natural that they be allotted to combat infections that proved readily susceptible. It has been only during the past year that sufficient quantities have become available for a comprehensive clinical appraisal of its value in non-gonococcal infections of the urogenital tract.

The response to penicillin in the non-specific urogenital infections is not so uniform as in the gonococcal infections but there is nevertheless a definite application in which the drug has proven spectacular. It is my purpose to discuss the use of penicillin in these urological conditions, indicating in broad general outlines how they may be recognized and how treatment should be carried out.

One of the cardinal principles governing the use of penicillin is to limit its application to pathogens which are susceptible. In some infections of the urogenital tract a bacteriological diagnosis cannot be made. In epididymitis or perinephritis, for example, there may be no involvement of the urinary passages or discharge of purulent exudate from which organisms can be recovered. One must then depend upon the clinical features of the case in assuming the type of the invading organism or use the drug empirically in order to determine its effect.

By now it is well established which bacteria are susceptible to penicillin and which are not. The most common penicillin-sensitive organisms encountered in non-specific urogenital infections are the streptococci and the staphylococci. Except for slight variations it is found that the beta hemolytic streptococci are very sensitive to penicillin. Streptococci viridans are moderately resistant and streptococci fecalis are still more resistant. The staphylococci are all more resistant than the streptococci as a group but practically all are susceptible to large therapeutic dosages. The pneumococci and the clostridium gas forming bacilli are penicillin-sensitive organisms less commonly seen in urologic practice.

### BACTERIA DEVELOP LITTLE RESISTANCE

If a group of organisms is sensitive to penicillin, one rarely encounters individually resistant strains. Furthermore, bacteria do not develop any

appreciable degree of resistance to penicillin while treatment is going on. In sulfonamide therapy, on the other hand, different strains of the same organism present wide variations in sensitivity and it is characteristic for bacteria which are originally sensitive to develop remarkable resistance to the sulfonamides during the administration of the drug.

Unfortunately the large group of gram negative bacilli which are common invaders of the urogenital tract are all refractory to such concentrations of penicillin as it is possible to attain in the blood and tissues. As a matter of fact, some of these bacilli are not only resistant to the drug but they actually destroy its effectiveness against other bacteria within very short periods of time; that is, within 12 hours or less.

Penicillin has been found to be ineffective in practically all virus infections. This is interesting from a urological point of view in that some observers are of the opinion that the abacterial infections of the urinary tract, which have attracted considerable attention during the past few years, are caused by a filtrable virus. I have observed over 15 cases of acute abacterial posterior urethritis and cystitis treated with 800,000 or more units of penicillin without a favorable response being elicited in any of the patients.

If it were purely a matter of determining whether or not a patient was suffering from an infection caused by a penicillin-sensitive pathogen, the treatment of the non-specific urogenital infections would be a simple matter. Such is not the case, however, for many non-specific infections of the urogenital tract from which penicillin-sensitive organisms are recovered, have proven refractory to the drug. In general it may be stated that penicillin has proven less satisfactory in infections of the urethra and seminal tract than in infections of the kidney and perinephric space. Some of the reasons for this apparent discrepancy have become obvious, others remain obscure.

### MORE EFFECTIVE IN ACUTE INFECTIONS

Hobby<sup>4</sup> and Dawson's experiments partially explain these clinical observations. They found that penicillin is most effective when rapid multiplication of bacteria is taking place. They noted that conditions which increase the rate of growth of bacteria, increase the rate at which penicillin acts. Conversely, conditions which decrease the rate of growth are found to decrease the rate at which penicillin acts. Reduced to simple clinical terms this means that penicillin is more effective in the acute infections than in the chronic, as has proven true in the treatment of infections in all parts of the body.

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This explanation helps to account for the fact that penicillin has proven useless in all cases of chronic non-gonococcal urethritis, epididymitis, prostatitis and seminal vesiculitis despite the fact that streptococci and staphylococci are the invading organism in many instances. It does not account for the poor response to penicillin in acute non-gonococcal urethritis, epididymitis, prostatitis and seminal vesiculitis. From a theoretical standpoint acute coccal infections of these organs should respond as promptly as similar infections in the kidney and perinephric space. Yet cumulating clinical evidence does not support this theory.

How can one explain the more favorable action of penicillin on renal infections? One obvious answer is that such large quantities of penicillin are excreted by the kidney that it is possible to obtain a greater concentration in the kidney than in other tissues of the body. Helmholz<sup>3</sup> and Sung have demonstrated that in the presence of normal renal function, 50 per cent of the injected daily dose is excreted in the urine. This may provide a partial explanation but it does not reconcile the difference in response between acute perinephritis on the one hand, and acute epididymitis or prostatitis on the other. If the concentration of the drug in the kidney were the sole factor, one would have to hypothesize that all perinephric infections are secondary to a primary infection in the kidney or that lesions which are presumed to be a perinephritis are in reality acute coccal infections of the kidney.

#### APPLICABLE METHODS

Having outlined the theoretical aspects, let us proceed to the practical considerations concerning the application of the drug. Most non-specific bacteria seen in urologic practice are so resistant that intramuscular administration provides the only satisfactory method of giving sufficient quantities of the drug. The efficiency of oral penicillin is so low that only one-fifth to one-tenth of the amount given is absorbed. We first believed that penicillin was destroyed by the acid in the stomach but later work indicates that the difficulty lies in the failure of absorption by the intestinal tract. It is difficult to impossible to obtain a high concentration by oral administration, to say nothing of the prohibitive cost. The intravenous route is unsatisfactory because it is followed by too rapid excretion and produces local irritation of the vein. Preparations in beeswax and oil reduce the need for frequent injections but they do not maintain as constant a blood level as injections of an aqueous solution every three hours. Three hours has been found to be the optimum time interval for intramuscular injection since the blood level falls rapidly thereafter.

There are no absolute rules governing the dosage of penicillin. In determining dosage, one must be guided by the sensitivity of the organism and the response of the patient. The sensitivity of the organism is indicated by its type but is more accurately assessed by in-vitro tests.

At present, four of the fractions of penicillin

recognized have been designated as G, F, X, and K. They are found in varying proportions in different commercial preparations. The biochemical properties of each fraction are only partially understood but it has been found that some organisms yield to one and not to another. This explains why some brands or lots prove effective in certain cases while others fail, and indicates that it may be valuable to test the sensitivity of an infecting organism to various preparations.

Most commercial preparations now contain a large proportion of penicillin K, usually about 50 per cent. Penicillin K apparently possesses the least antibiotic activity of the four fractions. Although it shows effectiveness in in-vitro tests, penicillin K is rapidly inactivated in the body. Producing companies are studying the problem and are attempting to improve the effectiveness of penicillin by increasing the content of penicillin G, one of the most potent forms. They are also seeking additional unknown fractions which are possibly being destroyed during the purification process. Until newer products become available, we can increase the concentration of the smaller fractions by increasing the total dosage being administered.

#### DOSAGE

For bacteria which are readily susceptible to penicillin the dosage should be from 100,000 to 200,000 units per day. In the serious infections it should be from 300,000 to 400,000 units per day. Usually maximum therapeutic concentration can be attained by giving 50,000 units every three hours, a total of 400,000 units per day.

It is a well known therapeutic axiom that if one gives a drug it is essential to administer it is sufficient amount to obtain a satisfactory therapeutic response. There is no difficulty in applying this rule to penicillin, for while there is no other known chemotherapeutic agent which is so powerful against bacteria, there is none which is so harmless to the host. This makes it possible to give enormous dosages without danger to the patient. In acute, fulminating infections, therefore, if the patient fails to demonstrate a prompt response the dosage should be increased at once. In the chronic infections, likewise, as soon as it becomes apparent that the patient is showing no improvement it is advisable to give larger amounts.

I will now briefly discuss the specific treatment of the various conditions which confront the urologist.

In acute perinephritis the patient should be started on not less than 25,000 units of penicillin every three hours as soon as the diagnosis is made. If, within 24 to 48 hours, there is no clinical improvement the dosage should be increased to as high as 50,000 units every three hours. In most instances there will be a dramatic response by the first or second day of treatment. In some patients the temperature falls by crisis, in others by lysis. If there is no improvement by the end of one week the chances are that a perinephric abscess has developed and that no amount of penicillin will remove the necessity for the surgical



drainage which is indicated. In eight cases the only patient who failed to respond had a large perinephric abscess.

The same dosage schedule applies to acute coccal infections within the kidney and the same response is to be anticipated. I have treated five cases successfully. It is extremely important to study the upper urinary tract in all patients with renal infection in order to rule out the possibility of a calculus, hydronephrosis, carbuncle or other condition which requires surgical intervention. This study should be delayed until the acute phase of the illness has been controlled, unless the patient fails to improve or grows worse when prompt investigation becomes imperative. Sometimes a plain x-ray shows the presence of a calculus, information that is of value in the further conduct of the case. In the presence of obstruction it is wise to treat the patient conservatively by draining the kidney with a ureteral catheter until the acute infection subsides. If this is impossible or proves inadequate, emergency operation is indicated.

Shearer,<sup>5</sup> Wiper and Miller report one case of renal carbuncle caused by hemolytic staphylococcus aureus which they treated successfully with penicillin combined with incision and drainage. The patient received a total dosage of 2,800,000 units over a period of two weeks, combined with an unstated amount used to lavage the abscess cavity. This experience indicates that it may no longer be necessary to resect or remove the kidney in renal carbuncle. It is reasonable to suppose that, if a coccal infection of the kidney is treated with penicillin sufficiently early, a carbuncle will not develop. In the case cited the patient had been having symptoms for two months and although he had been given a course of sulfadiazine he received no penicillin prior to operation.

After the acute febrile phase of a renal infection has subsided, therapy should be continued for several days. In the usual uncomplicated case the total dosage should be at least 2,000,000 units. Every effort should be made to prevent recurrence and to eradicate the infection before the stage is reached when the cycle of chronic disease becomes self-perpetuating.

#### PROLONGED PENICILLIN THERAPY

Once a chronic pyelonephritis has become established the prognosis for complete cure is poor. I have treated six cases of chronic staphylococcal pyelonephritis with penicillin for periods up to two weeks. In every patient the bacteria disappeared from the urine on dosages as low as 80,000 units per day but within a few weeks after cessation of treatment they invariably recurred. The danger of progressive secondary renal atrophy from a chronic pyelonephritis is so serious that I believe we are justified in placing these patients on really prolonged penicillin therapy, that is, to keep them on continuous administration for periods of six months or a year. In these cases the dosage required to keep the urine free of bacteria is usually so small that it should be possible to give adequate amounts by the oral route.

Penicillin sometimes proves valuable in mixed infections, for the body tissues may be able to control the infection after penicillin has eliminated the susceptible organisms. I found this to be true in a case of acute pyelonephritis of *b. coli* and hemolytic staphylococcus aureus etiology. Although the patient showed no improvement on large doses of sulfathiazol, when this was discontinued and the patient placed on penicillin there was immediate improvement. In other cases, either exclusively coccal or of mixed bacillary and coccal etiology, combined therapy, using both penicillin and one of the sulfonamides, may prove more effective than either drug used alone.

As concerns infections of the lower urinary and genital tracts, Thompson,<sup>6</sup> in 1944, reported a high incidence of improvement following one or two courses of 100,000 units of penicillin in the following non-specific lesions: 36 cases of urethritis, 30 of chronic prostatitis, four of acute epididymitis. As nearly as I can determine, no other urologist has observed such remarkable results in any of these conditions, certainly not with such small dosages of the drug.

This year Cooper<sup>7</sup> and MacLean report that 75 of 100 patients having chronic non-specific urethritis and prostatitis were cured upon two weeks' treatment with penicillin combined with prostatic massage. Their dosage schedule consisted of 2,800,000 units of penicillin given over a period of two weeks. All patients received at least one course. Some received two. Since these patients received additional forms of therapy such as prostatic massage, urethral dilatations, and endoscopic applications; since chronic urethritis and prostatitis are frequently subject to spontaneous remission, and since the criteria of cure in these conditions is far from clear-cut I am still not convinced that 2,800,000 units of penicillin, or double this amount, will produce any consistent improvement.

In my own experience I failed to note any beneficial response to penicillin in 35 cases of non-specific urethritis. These patients all had a urethral discharge produced by a staphylococcal or streptococcal infection in either the acute or chronic stage. They all received from 600,000 to 1,000,000 units of penicillin without any other form of therapy.

#### DIAGNOSTIC TEST

The failure in these cases has been so uniform that in awaiting culture reports in urethritis of questionable etiology one can rely, for all practical purposes, on the administration of penicillin as a therapeutic diagnostic test. A course of 200,000 units will elicit a prompt diminution or cessation of the urethral discharge produced by the gonococcus but can be depended upon to have no effect upon a non-gonococcal urethritis, either abacterial or non-specific. In a gonococcal infection complicated by secondary invaders, some improvement is usually noted although a prompt cure does not always result.

I believe that our experience has been sufficient to prove that any form of penicillin so far de-



veloped is useless in non-gonococcal urethritis. It is now my practice never to give penicillin in a non-specific urethritis unless the diagnosis is questionable. In these cases it may be worth while to give a course of 200,000 units.

My results in acute non-specific prostatitis and epididymitis have been more encouraging. Of eight cases of acute prostatitis, two showed improvement; of ten cases of acute epididymitis, three were improved. In all the patients showing improvement, staphylococci were recovered from the urine. I am convinced that the dosages in this series of cases, ranging from 160,000 to 800,000 units, were too small. Acute lesions in the epididymis and prostate apparently represent very resistant infections and I am anxious to see if these results cannot be improved by giving 50,000 units of penicillin every three hours up to a total dosage of 3,000,000 to 4,000,000 units.

In eight cases of chronic prostatitis and two of chronic epididymitis no improvement was noted in dosages of from 160,000 to 1,000,000 units.

Penicillin has proven invaluable in the treatment of postoperative wound infections. When cocci are the invading organism, experience has shown that if the drug is started at once the wound will not break down and healing will be prompt. Usually 200,000 units of penicillin a day is a sufficient dosage. I was particularly impressed with one case of a severe, diffuse hemolytic staphylococcus aureus wound infection following an orchidopexy I performed with cotton suture material. Not only was healing rapid and complete but not one of the sutures sloughed out.

The use of penicillin should improve our results in plastic operations on the penis and urethra and in muscle transplants. Cordonnier<sup>2</sup> states that he has been able practically to eliminate infection in the repair of hypospadias by the combined use of sulfadiazine and penicillin both pre- and post-operatively.

A danger incident to the use of penicillin is that too much reliance may be placed in the drug, leading to the neglect of careful diagnosis and observation of the patient. While being a valuable adjunct to treatment, penicillin does not take the place of well timed surgical procedures, transfusions, serums, antitoxins and proper medical measures. It is the responsibility of the urologist

to recognize such complicating factors as poor urinary drainage, the presence of calculi, the development of abscesses, and to treat these conditions as indicated.

In summary it may be said that while the most dramatic results have been obtained in the acute infections, good results may be possible in some chronic infections by more prolonged treatment. Regardless of the lesion, the guiding principles of treatment are to begin penicillin early, to give it in adequate amounts and to continue therapy until the body has destroyed all causative organisms. By starting treatment early it is possible to prevent irreparable damage and to avoid the development of irreversible pathological changes. By continuing treatment for a long time after the febrile reaction has subsided, one prevents recurrences and the development of residual chronic infection.

#### SUMMARY

Although the value of penicillin in treating gonococcal infections has been well established, considerable obscurity still exists as concerns the use of this drug in non-gonococcal infections of the urogenital tract. The subject is discussed, differentiating those urological lesions which are susceptible from those which are not. Certain principles of treatment are evolved, on the basis of the type and location of the infection, the infecting organism and the effective dosage.

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## The Trend of Medicine and Its Relationship To the Prevention of Disease\*

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BEFORE the time of Hippocrates, the practice of medicine was a matter of objective diagnosis, and during its early evolution some emphasis was placed on therapeutics. Subsequently attention was directed toward refinements in diagnosis, and by the twentieth century, diagnosis had become a relatively precise science. Ultimately therapeutics also became reasonably accurate, based as it was upon better knowledge of anatomic change and compensatory physiologic adjustment. In both circumstances the emphasis was placed on man in an abnormal state of health.

Today more is demanded of the physician than an interest in disease alone, for the practice of medicine transcends both diagnosis and therapeutics, which by themselves do not answer the modern challenge. At present it is demanded that the physician expend more effort toward the prevention of disease, thereby placing emphasis on understanding those factors which maintain man in equilibrium with his environment, rather than on those which precipitate illness. The physician is compelled to recognize the importance of the interaction of those situations which impinge upon and affect the equilibrium between man and his surroundings. Physicians of necessity must become philosophical biologists in order to have the maximum comprehension of the trend of medicine.

Unfortunately the curricula of modern medical schools have been over-burdened with the techniques of specialization and the minutiae of the sciences ancillary to medicine, and for that reason the more important subject of ecology has been excluded.

Because of the scientific advances in the conservation of health, more persons are allowed to live today than could have hoped to have survived a century ago. As a result the need for physicians with a philosophic viewpoint of biology becomes imperative. What crimes are committed under the license of science! One thing is certain, we shall perish or lose our leadership in direct proportion to our ignorance of those immutable laws which govern the actions and reactions of the human organism as it seeks to express itself in its environment, whether that be biologic, social, economic, or psychologic.

The categorical statement can be made that the

vocation of the physician should be the study of human beings seeking adjustment in their environments, his avocation the study of disease in individuals and in populations. The physician's vocation, then, impels him to study human ecology. In its essential nature ecology is the observation, enumeration, testing and synthesis of whatever can be known about life and environment, in order to interpret the relationships existing between them in practical terms.

An inquiry into the chain of events that makes the independent human being totally dependent in time and space upon his environment is of necessity an inquiry into human ecology. In fact, the human subject is absolutely dependent upon the most minute and apparently insignificant factors of his environment. He is a part of all he experiences, and disease is often the folly of an avoidable, unpleasant experience. If the physician were to know what elements of the external environment condition the human subject both qualitatively and quantitatively, he would be better prepared to assess the defense reactions of the internal environment, and thereby understand more fully the mechanisms of the production of disease in the individual.

How can a man be advised and treated for an internal, physiologic adjustment to an aberrant external stimulus if the physician fails to appreciate or is unaware of the part which environment and habit plays in the life of man? The physician should strive to know more about normal man, so that he will be able to understand the subtle factors which lead to devitalization and ultimate illness. Often in the search for the specific cause of disease, contributing elements such as psychologic conditioning, avoidable social pressures, insufficient leisure, poor nutrition, and other inevitable ecologic factors are overlooked.

One of the most important of these is the study of nutrition. Either too much or too little food may produce illness, and the intelligent application of the proper dietary regimen may cure it. Through application of the principles of good nutrition, emphasis is automatically placed on keeping man well. The expert in nutrition can advise what to eat, and why it should be eaten, but until the part which poor nutrition plays in the etiology of disease is appreciated, recognized and understood, this important causative factor of devitalization cannot be successfully combated or prevented. There is much hidden hunger in our land of plenty, much devitalization that goes unheeded, and much disease that is unrecognized.

The time for a careful re-evaluation of the need for prevention of disease is imminent. Diag-

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nosis and treatment without prophylaxis and prevention are indeed sterile. What the physician of the future needs is a more than passing acquaintance with biology and a quickened interest in the study of human ecology. What more practical step toward the solution of this dilemma could be designed than the establishment of an Institute of Human Nutrition where the practicing physician could become acquainted with the interaction of agricultural, biologic, geographic, economic, sociologic and psychologic situations which comprise and condition the equilibrium existing between the external and the internal environments of man. The physician must appreciate that medicine in all of its ramifications is a social science, and that his services to society should be consonant with this thesis. A life in which human conservation becomes the major goal should be

the purpose of all of our activities. Any individual who is needlessly wasted or neglected constitutes not only a preventable loss, but an affront to human dignity and a negation of the principle of a free and democratic society.

In summarizing these discursive remarks on the trend of medicine and its significance to the physician, the conclusion is evident that the prevention of disease is assuming greater proportion in our modern world and that the subject matter of diagnosis, treatment, and the prevention of disease should have at *least* equal emphasis in the medical curriculum. Within the field of prevention the theme of human ecology should permeate its entire philosophy, and a first step toward this ideal could be achieved by means of a thorough exploration of the subject matter of nutrition in its relationship to man.

## The Clotting Mechanism and Tests For Its Efficiency\*

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ANYONE who has attempted to review, even most superficially, the literature on the subject of coagulation must be impressed by the tremendous amount of effort that has been expended in the attempt to solve this problem. Theories and more theories have been proposed and arguments between the proponents of the theories have waxed long and loud. Now the modern concept of the clotting mechanism may be presented in its simplest terms as follows:

Thromboplastin + prothrombin + calcium = thrombin. Thrombin + fibrinogen = fibrin. This is our classical theory and is the best working hypothesis that we have. Yet even it does not explain all the problems of the coagulation mechanism, nor do all investigators accept it, at least not in this simple form. It is, of course, this skepticism that stimulates investigation and adds to our knowledge, but in this brief review we cannot discuss fully the disputed points.

What are these substances which we consider essential in this process? Thromboplastin has never been isolated and purified and we know it better by its activity than by any other of its properties. We know that it is a substance which occurs in platelets and in many tissue cells, and we know that it is essential for the conversion of prothrombin to thrombin. It does not occur in circulating blood or at least not in significant amounts. It is set free when platelets disintegrate from any cause, or when tissue is damaged. It is

quite stable when exposed to heat and for that reason it probably cannot be considered to be an enzyme.

Prothrombin is thought to be a protein containing a considerable amount of carbohydrate. It is produced by the liver, possibly to some extent by other tissues. That the liver is the most important source can readily be shown experimentally by causing damage of the liver, following which the prothrombin content of the blood rapidly decreases. For its production, there must be available to the liver an adequate supply of natural Vitamin K or a satisfactory methyl naphthoquinone derivative. The prothrombin of the newborn may be normal or below normal at birth, but regularly the level falls for a few days usually returning to normal by the end of the first week when the intestinal bacterial flora becomes established and produces Vitamin K. If the level falls too low, hemorrhagic disease may occur.

Thrombin results from the activation of prothrombin by thromboplastin in the presence of calcium. It has been shown that a fixed amount of prothrombin yields a constant amount of thrombin, irrespective of the excess of thromboplastin added. Thrombin has been shown to be a protein which also contains carbohydrate. While there is no doubt that calcium is indispensable in the conversion of prothrombin to thrombin, there has been much disagreement as to the role that it plays. It is, of course, by the addition of such substances as the oxalates and citrates which remove or fix the calcium of the blood that clotting is most frequently prevented in blood withdrawn for the purpose of investigation or for trans-

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fusion, yet it is known that considerably more oxalate must be added to blood than is sufficient to precipitate the free calcium in order to prevent coagulation. This suggests that calcium may be in combination with prothrombin and that the excess of oxalate may be necessary to release it from this substance. Thrombin certainly does not contain calcium.

The rate of coagulation depends upon the concentration of thrombin and by the same token upon the concentration of prothrombin present before its conversion to thrombin. The manner in which thrombin changes fibrinogen to fibrin is like an enzymatic or catalytic action. Thrombin does not combine with fibrinogen and it has been shown that a purified preparation of thrombin is able to convert over 200 times its weight of fibrinogen to fibrin. After coagulation of blood a high concentration of thrombin is present in serum but this thrombin activity rapidly disappears. Yet, by appropriate methods, it can be reactivated which suggests that it combines with some other serum constituent.

We should not forget that certain changes take place in the clot after coagulation. The clot contracts and this process can be observed best when the blood is allowed to coagulate in a test tube. When the clot contracts, serum is expressed. This phenomenon appears to be due to the presence of platelets which become adherent to the strands of fibrin and in some way cause them to bend and distort. As is well known, a great reduction of platelets in blood destroys the ability of the clot to retract. In addition to this role and that of furnishing thromboplastin, the platelets play an important role in intravascular clotting. Indeed, the platelets initiate thrombosis by attaching themselves in large numbers, usually in clumps, to the point of damage of the lining of the blood vessel. As soon as they adhere to the damaged surface, they seem to become sticky and by this property appear to assist in attaching fibrin to the lining.

Fibrinogen is classified as a globulin. It is different, however, from the other proteins of the plasma, as is obvious when we consider its action when thrombin is formed in blood plasma. It appears to be formed in the liver. However, it does not decrease in the circulation nearly so rapidly in the presence of liver damage as does prothrombin. It is rare that there is sufficient variation in the concentration of fibrinogen to interfere with the process of coagulation. Calcium is even more rarely reduced to a level low enough to retard the clotting mechanism.

There are two procedures which are of the greatest importance in estimating the efficiency of the clotting mechanism. These are the determination of coagulation time and the determination of the amount of prothrombin present. While the determination of the bleeding time and the estimation of platelets are important in any hemorrhagic disease, they are not so directly concerned in artificial control of the clotting mechanism. There are many methods for the determination of the coagulation time, but probably the best for clinical

purposes is the one known as the Lee-White method, in which blood obtained by venipuncture is placed in the amount of 1 cc. in a small dry clean test tube 8 mm. in diameter. Ordinarily, two or three tubes are used and one or two of these are tilted every 30 seconds until a clot is formed which is sufficiently solid to allow inversion of the tube. The second or third tube acts as a control upon the one which is tilted. The blood should be kept at approximately body temperature. Normal blood varies in its coagulation time by this method over a fairly wide range, from six to fifteen minutes. The blood should be obtained by a clean rapid venipuncture and suction should be avoided. These precautions minimize the introduction of thromboplastin from the tissue.

When venipuncture is not feasible, probably the capillary tube method is next best. Here a capillary tube 1 mm. in diameter is filled with blood obtained by skin puncture. Every 30 seconds the tube is filed and a small piece is broken off. The end point is determined by the period at which a fibrin thread is seen between the separated fragments. The normal time is from three to seven minutes. This method is subject to the objection that by skin puncture, a considerable amount of thromboplastin is released and mixed with the blood. The determination of coagulation time is of greatest importance in the diagnosis of hemophilia and in the control of heparin therapy, otherwise the determination of coagulation time is of little value. I feel that an enormous amount of time is wasted in the clinical laboratory in the performance of this test.

For the estimation of prothrombin activity the method of Quick is most frequently used. It is simpler than the two stage method of Wamer, Brinkhous and Smith and more accurate than the so-called bedside methods. Briefly the steps in this procedure are as follows: 4.5 cc. of blood are obtained by venipuncture and are mixed with 0.5 cc. of 0.1M sodium oxalate. This prevents coagulation and this blood is then centrifuged and the plasma is used for the test. 0.1 cc. of the plasma is mixed with 0.1 cc. of thromboplastin in a small test tube and placed for one minute in a water bath at  $37\frac{1}{2}^{\circ}$  centigrade. Then, 0.1 cc. of 0.02M calcium chloride is added. The tube is first shaken, then gently tilted back and forth until the clot forms and the time required for the formation of the clot is determined by the use of a stop watch. One or more normal controls are always used and for accuracy every determination should be checked. The thromboplastin used is dehydrated rabbit brain. Quick says that the coagulation time of normal plasma by this method should be from 11 to  $12\frac{1}{2}$  seconds. This depends upon the use of an active thromboplastin, and it is in the preparation of the thromboplastin that many laboratories appear to have difficulty. At any rate, many are unable to produce a thromboplastin which will cause coagulation in  $12\frac{1}{2}$  seconds. However, a somewhat less active thromboplastin may be used and accurate results obtained.

Quick<sup>1</sup> describes a method for the determina-



tion of the potency of the thromboplastin when it is not up to the highest standard of efficiency.

TABLE 1

Concentration of prothrombin in plasma, %	Clotting Time	
	Undiluted plasma sec.	Diluted plasma* 50% sec.
100	11-12	15
97	—	15½
90	—	16
85	—	16½
80	12½	17
75	—	17½
70	—	18
67	—	18½
65	—	19
60	—	19½
58	13½	20
56	—	20½
53	—	21
50	15	21½
40	17	—
30	19½	—
25	22	—
20	25-26	—
10	37-40	—
5	55-65	—

\* The plasma is diluted with an equal volume of physiologic saline solution.

The prothrombin time of the unknown plasma is determined and the theoretical percentage of prothrombin read from the table or graph. Normal plasma is diluted 50 per cent with physiological salt solution and its prothrombin time determined. This should be 15 seconds with an active thromboplastin, but if it is more than 15 and less than 22, its percentage activity can be found opposite the figure obtained in the left hand column. Thus, if the figure obtained with diluted normal plasma is 21.5, the thromboplastin is 50 per cent active. If the prothrombin time of the unknown is 22 seconds, the theoretical value of the prothrombin content is 25 per cent, but since the thromboplastin is only 50 per cent active, the actual value is 25 per cent divided by 0.50, or 50 per cent. Attempts to find a more stable thromboplastin than dehydrated rabbit brain, have been

made by many. Russell viper venom was found to have an active thromboplastic action, is quite stable and is used by many laboratories.

A relatively small prolongation of the coagulation time of the plasma by Quick's method indicates a considerable decrease in the prothrombin activity. This is shown by the well known graph prepared by Quick (Figure 1), as well as by the table above.

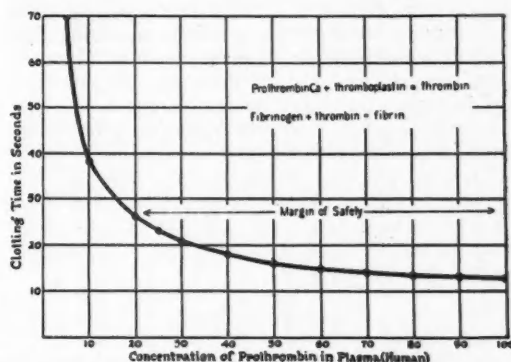


FIG. 1. Human prothrombin curve. The relation of the coagulation time of recalcified plasma (with excess of thromboplastin) to the concentration of prothrombin.

There is a wide range of safety as far as hemorrhage is concerned in the percentage reduction of the prothrombin activity and there is little danger of hemorrhage before the prothrombin is reduced to 20 per cent of normal. However, when the prothrombin level is deliberately reduced as by the use of dicumarol, effective levels for the prevention of thrombosis are readily reached before this danger point is approached.

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## Delayed Reactions Following Penicillin Therapy\*

### PRELIMINARY REPORT

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AS penicillin has become more widely used, reports dealing with reactions occurring during its administration have appeared with increasing frequency.<sup>1,2,5,6,7,8,9</sup> However, examination of literature has failed to reveal any detailed account of delayed reactions occurring after cessation of penicillin therapy.

It is the purpose of this report to describe seven cases in which reactions, varying in severity from mild to extremely severe, appeared at intervals of two to twenty-eight days after the last administered dose of penicillin.

### REPORT OF CASES

**CASE 1:** A 49-year-old white male entered the hospital for penicillin therapy of latent syphilis. He had been known to have a positive Wassermann for the past 19 or 20 years, but he gave no history of primary or secondary lues. He had had sporadic mapharsen and bismuth therapy during the last five to six years, and both drugs had caused typical skin reactions. No history of asthma, hay fever or urticaria was obtained. Other than the positive Wassermann and Kahn tests, there were no other important physical or laboratory findings. Spinal fluid Wassermann test was negative.

He was given 3,000,000 units of sodium penicillin in divided doses intramuscularly over a period of seven days and was then discharged. His course remained uneventful until three days after the last injection of penicillin, at which time he re-entered the hospital because of intensely pruritic giant hives over the entire body. Symptomatic therapy with calamine lotion, calcium gluconate intravenously, ephedrine orally, and epinephrine intramuscularly gave the patient little relief. He became edematous over the entire body including head, palms and soles. By the third day, a gnawing epigastric pain appeared accompanied by nausea and vomiting. These gastrointestinal symptoms were promptly controlled by milk and alkaline water. The temperature went up as high as 40° C. The following day he complained of severe headache and neck stiffness, and became delirious. Urinalysis at the onset of this reaction contained one plus albumin but was otherwise normal. There was a slight leukocytosis of 12,000 with 90 per cent polys and no eosinophiles. Edema and urticaria slowly subsided and the patient became asymptomatic ten days after the onset of the reaction.

**CASE 2:** An 85-year-old white male with generalized arteriosclerosis and hypertension entered the hospital because of a septic sore throat. Physical examination revealed a moderately severe acute pharyngitis. On entry the white blood cell count was 10,000 with 74 per cent polys, 17 of which were stab cells. He was given 25,000 units of penicillin every three hours, and after two days of therapy a scarlatiniform eruption appeared over the

entire chest and abdomen. Penicillin treatment was continued for three more days in spite of the eruption, but was abandoned because of intense pruritus. A total of 1,295,000 units had been given. The patient was discharged three days later after the eruption and urticaria had completely subsided.

Four days after discharge the patient developed giant ecchymoses over the entire body. These were most pronounced over the injection sites on the buttocks and were also accompanied by intense pruritus. There was no leukocytosis, nor any reduction of hemoglobin or platelet count. Treatment was symptomatic and convalescence required three weeks.

**CASE 3:** A 50-year-old white male entered the hospital because of a low back injury with nerve root irritation in the lumbar region. A limited fusion of the lumbosacral area was performed and subsequently a superficial wound infection due to staphylococcus aureus developed. Healing was obtained after about 1,000,000 units of combined local and intramuscular penicillin, and he was discharged one and a half months after entry.

Approximately ten months later, a draining sinus developed in the central portion of the lumbar wound, and he was re-hospitalized. The old scar was excised, the tract traced down to a silk suture in the superficial fascia, and 20,000 units of penicillin was placed in the wound before closure. The patient was also given 15,000 units of penicillin intramuscularly every three hours for seven days, then decreased to 5,000 units every three hours for another day. He was discharged on the 19th hospital day.

The patient returned to the hospital four days after discharge, stating that giant hives had developed two days after cessation of penicillin therapy. On examination, advanced urticarial lesions were found over the body, scalp and extremities, and the hands and feet were markedly edematous. Urinalysis and blood count were normal. The patient died on the fourth hospital day of toxemia from a gas bacillus infection which developed 36 hours before death. The source of the infection was not determined.

**CASE 4:** A 30-year-old white male received 1,000,000 units of penicillin orally given every three hours for one week, for a chronic rectal fistula. Two days after cessation of therapy, giant hives appeared over both palms and then over the thorax and extremities. Markedly painful edema of both soles appeared and he was unable to walk. Temperature rose to 39.4° C. accompanied by dyspnea and palpitation. This reaction was moderately severe, but he was able to remain at home and recovered in two weeks with symptomatic therapy.

This patient gave no history of previous asthma, hives or eczema. He had received 15 injections of penicillin (dosage unknown) one year before with no untoward effects.

**CASE 5:** A 44-year-old white female was hospitalized because of a severe pruritus vulvae and ani. A total of

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540,000 units of sodium penicillin was given in 30,000 unit doses every three hours.

Twenty-eight days after the last penicillin injection, the patient had a sudden onset of severe pruritus and urticaria about the neck; these rapidly spread to the chest, abdomen, and extremities. There was also a severe "vice-like" headache, low mid-abdominal pain, and dysuria. She could not walk because of pain and swelling of the feet. During the first three days of the reaction the temperature ranged from 38.8° to 39.4° C. and complete recovery required two weeks.

This patient gave no history of allergic manifestations or previous penicillin therapy.

**CASE 6:** A 30-year-old white female was hospitalized for menorrhagia of two months' duration. A left salpingo-oophorectomy was performed because of tubal pregnancy. During the operation 500 cc. of whole citrated blood was given. On the eighth post-operative day she developed a left femoral phlebitis for which she was first given sulfadiazine without improvement, and then 2,760,000 units of penicillin intramuscularly over an 11-day period. Recovery followed and the patient was sent home on the 31st post-operative day. Seven days after penicillin therapy had been discontinued, she developed giant urticaria of the face, hands, arms, thighs, and back, with moderately severe pruritus. She was given ephedrine orally, and in four days she was asymptomatic. This reaction was comparatively mild. There had been no previous penicillin treatment but there was a history of asthma from infancy to the age of 14, with no allergic manifestations for the last 16 years.

**CASE 7:** A 29-year-old white male had been in good general health with no past personal or family history of allergy, urticaria, or arthritis. Sodium penicillin, in a total dosage of 400,000 units given intramuscularly every three hours over a three-day period, was instituted for a moderately severe purulent bronchitis accompanying an influenza-like infection. Prompt drop in fever from 38.8° C. to normal with clearing of purulent sputum occurred on the last day of therapy.

The patient rapidly became asymptomatic and remained so until nine days after the last dose of penicillin, when an abrupt onset of marked redness, tenderness, swelling and pain in the soft tissues about both wrists and the small joints of both hands was noted. Twenty-four hours later diffuse, intensely pruritic, giant urticarial wheals appeared over most of the body. Joint involvement then spread to both knees and shoulders, and tender 3x3 cm. deep subcutaneous nodules appeared adjacent to these joints. Mild hydrarthrosis of the left knee followed. The soles of both feet, and both dorsi and palms of the hands, became hot, painfully edematous, and redenned, and edema of the eyelids and posterior pharynx ensued. The temperature rose to 38.8° C., and the patient became quite incapacitated. There was a leukocytosis of 14,200, with a normal differential count, and the urinalysis was normal.

No relief was obtained from the usual measures, including oral ephedrine and amytal, multiple injections of 1:1000 epinephrine, and intravenous calcium gluconate. "Benadryl," 50 mgm. twice daily (oral), produced relief from pruritus but had no effect upon edema or joint pain.

Slow subsidence of joint swelling, redness, and tenderness with gradual disappearance of nodules and urticaria occurred. All signs and symptoms had completely disappeared ten days after the onset of the reaction.

#### COMMENT

As can be seen in the accompanying table, reactions were unrelated to the duration or quantity

of penicillin, and occurred after oral as well as after intramuscular administration. The one case

Case	Total Units Penicillin	Route of Administ.	Duration of Treatment	Interval between last dose and onset of reaction
1.	3,000,000	Intramusc.	7 days	3 days
2.	1,300,000	Intramusc.	5 days	7 days
3.	900,000	Intramusc.	8 days	2 days
4.	1,000,000	Oral	7 days	2 days
5.	540,000	Intramusc.	2½ days	28 days
6.	2,760,000	Intramusc.	11 days	7 days
7.	400,000	Intramusc.	3 days	9 days

which reacted after oral therapy had received parenteral penicillin one year before. One further case we are aware of developed mild but diffuse urticaria seven days following the testing of a penicillin aerosol apparatus, with inhalation of an estimated 5,000 units. Thus it is likely that this route of administration, as well as oral and intramuscular routes, is not free from delayed effects. It is significant that the majority of these patients gave no allergic histories, and did not suffer from fungous "id" reactions.<sup>8,4</sup> Reactions were considered severe in six out of the seven cases, producing systemic as well as local manifestations. Systemic reactions consisted of fever, prostration, gastro-intestinal symptoms, severe headache, mild leukocytosis and albuminuria. Local reactions varied with the severity of the process and consisted of diffuse giant urticaria, intense pruritus, scarlatiniform eruption, severe arthralgia, hydrarthrosis, ecchymosis, and the formation of tender deep subcutaneous nodules resembling those seen in erythema nodosum. One or several of these local manifestations could be seen in the same patient. The general picture in two cases resembled that seen during severe serum reactions.

Studies of penicillin sensitivity occurring during therapy, or on re-administration of the drug, seem to indicate that true allergy to penicillin does occur.<sup>8,9,2,1,3</sup> Why the manifestations should be so long delayed, as illustrated by this report, requires further study.

It is not our purpose at this time to discuss in detail the possible mechanisms involved in these delayed reactions. However, we consider them striking enough to warrant description. Awareness of their occurrence with the possibility of one or more weeks of incapacitation demands circumspection before penicillin is prescribed for illnesses which would otherwise run a self-limited course.

#### SUMMARY

1. Seven cases of delayed reactions following penicillin administration are reported.

2. Reactions included urticaria, joint involvement, ecchymoses, gastro-intestinal and central nervous system manifestations. Severity of the reaction was not related to the amount or route of administration.

3. Delay in appearance of these reactions

varied from two to twenty-eight days after cessation of penicillin therapy.

4. Incapacitation resulting from the reactions averaged about two weeks.

5. Circumspection regarding use of penicillin in otherwise self-limited illnesses, and its reservation for use only in disease processes with well defined indications, is urged.

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#### DOCTORS REPORT TWO CASES OF RARE DISEASE CARRIED BY RATS

A new complication of a heretofore rare rat-borne disease, the first of its kind to be recognized in the United States, is reported in the August 17 issue of *The Journal of the American Medical Association* by three Rochester, N. Y., physicians.

They state that they treated two patients suffering from a kidney infection caused by leptospiral organisms which are carried by rats. This infection usually affects the liver.

The authors—W. W. Stiles, M.D., J. D. Goldstein, M.D., and W. S. McCann, M.D., from the Departments of Bacteriology and Medicine of the University of Rochester School of Medicine and Dentistry—state that "instances of this 'pure' renal form of leptospirosis are fairly common abroad, but prior to this report no cases have been recognized in the United States. The two patients observed in Rochester are the first confirmed instances of anicteric leptospiral nephritis to be reported in this country."

The first patient was a schoolboy, aged 17, who had symptoms of vomiting, diarrhea, headache, severe backache and a temperature of 103 F. He had been swimming almost daily in the Erie Barge Canal near Pittsford, N. Y., and although the canal was known to be infested

with rats he was not aware of any direct contact with the rodents. He was aware that water had entered the upper respiratory passages on several occasions. He was discharged from the hospital on the 19th day after the onset of his illness and remained in bed at home for an additional five weeks. The patient was treated with a high protein, salt free diet, and given a large amount of fluids.

The second patient was a dairy worker with the same general symptoms. The article points out that "for the past several years the patient had worked in a milk pasteurizing plant in Pittsford, N. Y. He said that rats were frequently seen about the plant and that approximately three weeks before this illness one of them had become caught in the mechanism of a bottle washer, and its macerated tissues had been thrown about and over him." Fever persisted until the 16th day of illness in this patient. He remained in bed two weeks at home after discharge from the hospital.

The infection was discovered in both instances after a total of 60 guinea pigs were used in testing the bloods of the patients. The guinea pigs are very susceptible to leptospira.





# California MEDICINE

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## EDITORIALS

### Can We Predict the Therapeutic Effect of the New Radioactive Elements?

"CHILD flown across continent to get atomic treatment for leukemia—only to find deadly disease cannot be cured by radioactive bombardment," is the gist of a recent article by United Press. With a tremendous and quite logical public interest in atomic developments, we can perhaps expect that such incidents which have occurred with fair regularity in the past will now make headlines even oftener. It is indeed stirring to the imagination of layman and doctor alike to consider that some of the radioactive isotopes which can now be produced in relatively large quantities in the atomic pile may prove the cure to hitherto hopeless diseases.

Has our experience so far been sufficient that we can predict the course that such treatment will take and its outcome in some diseases? The answer is an unqualified "yes." It is now some ten years since radioactive phosphorus was synthesized in the cyclotron, and there has been a steady trickle of reports on the effect of radioactive isotopes in the treatment of leukemia and other malignant diseases ever since. Regarding the systemic effect of radioactive substances introduced intravenously or by mouth into the human being, we have known the answer for more than thirty years, for it was inevitable that investigators would try the effect of small doses of radium or radon on the entire organism, as well as apply relatively larger amounts to localized malignancies. Cameron<sup>1</sup> in 1915 classified the various methods of internal administration which ranged all the way from inhalation of radon containing steam to radium enemas. Then, as now, the idea seemed attractive that even a small dose of a substance with such concentrated power as radium might somehow produce a desirable effect.

The answer was not long in coming. Even if we had forgotten results of thirty years ago, the watch dial painters who pointed the tips of the radium-containing brushes with their lips gave an involuntary demonstration of the effect of radium

poisoning in the early part of this decade.<sup>4</sup> Even earlier those of the gullible who responded to advertisements ballyhooing the beneficial effects of the waters from radioactive springs found out personally about radium poisoning the dangerous way.<sup>2</sup>

We have abundant information, therefore, to predict the systemic effects of radioactive substances introduced into the body.<sup>5</sup> As is always true with radiation therapy, there is a destructive effect which is differential in character depending upon the growth characteristics of the various cells. The most rapidly growing cells are the first to succumb to effect of radiation. The blood cells are particularly vulnerable, and experiments using Phosphorus 32 in the control of leukemia have been conducted with a degree of success for more than ten years.<sup>3</sup> Likewise, the "circulating tumors" of the blood stream which involve the red cells—polycythemia vera—respond to intravenous P-32. Edward H. Reinhard at the recent meeting of the American Association for the Advancement of Science, reports that P-32 in the treatment of polycythemia vera is "probably the best therapeutic agent at the present time."

Working at the Philadelphia General Hospital, Widmann<sup>6</sup> recently reported a large series of leukemia patients treated by all the radiation methods now generally used. Whether he irradiated bone marrow or spleen or set the patient at a distance from the x-ray tube so that the entire organism could be "sprayed" he got the same result. In brief, there was no response in cases of acute leukemia, but the chronic cases responded by palliation of symptoms and a lengthening of life which Widmann adjudged to be about a year.

In a recent report to the American Radium Society and elsewhere, Dr. John Lawrence, who has worked for ten years with radioactive elements produced by the cyclotron, expressed the opinion that the therapeutic results were no better than those produced by x-ray.

It is entirely reasonable to conclude that in leukemia the new radioactive substances have nothing new to offer. Any type of radiation palliates chronic leukemia. No type seems to benefit in the acute cases.<sup>6</sup>

This does not mean that we cannot look forward to much of great scientific interest and possible therapeutic help from radioactive elements. Such isotopes, previously produced by the cyclotron in amounts detectable only by ultramicrochemistry, can now be expected from the atomic pile in sufficient quantity to render them available for medical experimentation. Radioactive phosphorus is concentrated in organs with a high phosphorus content such as bone, but experiments in the control of osteogenic sarcoma have been disappointing, because it has not been possible to reach a sufficiently high concentration in the tumor area. Radioactive iodine is concentrated in the thyroid, and early experiments show it may be very useful in the control of hyperthyroidism, or even sometimes in the control of thyroid carcinoma.

P-32 has a half life of 14.3 days—a fact which may make it much more useful than radon, which is customarily used for implantation in gold seeds, and which has a half life of a little less than 4 days. Low-Beer<sup>8</sup> has recently used blotting paper moistened by P-32 to cure surface malignancies.

There are numerous interesting possibilities for

the use of radioactive isotopes, many yet unexplored. We can predict with reason and from more than ten years' experience, however, that there will be no advantage in the use of these substances over the commonly used types of radiation in the treatment of leukemia.

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### FREEDOM FROM DOUBT

When the California State Supreme Court late last month issued its decision in the California Physicians' Service case it removed whatever doubt had previously existed as to the exact corporate structure and status of C.P.S. Litigation lasting more than six years was concluded and the doctors behind the program were given a green light to proceed under their original plans.

Behind this case was the desire of C.P.S. to prove itself a service organization, incorporated not for profit but for the good that could be delivered to the people of California. The original suit was filed in Superior Court by C.P.S., asking that the court declare C.P.S. not an insurance operation. The Superior Court agreed with the reasoning behind this suit and enjoined the state Insurance Commissioner from assuming jurisdiction over C.P.S.

On appeal from this decision by the Insurance Commissioner, the Appeal Court upheld the Superior Court; on appeal from that decision, the matter went before the Supreme Court.

On another page of this issue will be found a digest of the Supreme Court decision; it makes extremely interesting reading. For the benefit of those who do not wish to go over the entire digest, it is noteworthy that the Court looked upon C.P.S. from the human side and not merely from the business angle. The decision says:

"Probably there is no more impelling need than that of adequate medical care on a voluntary, low-cost basis. The medical profession, unitedly, is endeavoring to meet that need. Unquestionably this is a service of a high order and not indemnity."

In another place the Court characterizes C.P.S. as "a pioneer attempt by the physicians of California to make available medical care for those who find the cost of sickness a burden not easy to bear."

One result of this opinion is that there need now be no question about imposing on the people of California a gross premiums tax which would be levied against them if C.P.S. were held to be an insurance operation. Thus a tax on human suffering need not be levied. Another result is that the many corporations and business organizations which have been hesitant to enroll their employees in C.P.S. because of a possible cloud on the status of the service may now go ahead and bring the benefits of a high grade non-profit medical care service to their workers.

As for the doctors—and more than 7,400 of them are now physician members of C.P.S.—the most significant interpretation of this decision is the removal of doubt which has shadowed C.P.S. for six years. Wherever hesitancy may have existed before, it may now be dropped;

wherever questions arose as to just what corporate form C.P.S. may have occupied, there is now an answer.

The Supreme Court has given its opinion, a green light. The enrollment drives now being staged may continue without interruption. The

more than 265,000 present beneficiary members may be assured that their medical care is forthcoming and that the new members swelling C.P.S. membership rolls each day will receive the same high quality medical service on a non-profit co-operative basis.

### **Study of Child Health Services**

The American Academy of Pediatrics has undertaken and now has begun a nationwide Study of Child Health Services. As the study gets under way in California, its sponsors are asking and surely should be given the full cooperation of physicians who are being called upon for needed factual information. It has the approval of the California Medical Association as well as of other organizations of physicians.

Purpose of the study is two-fold: (1) to collect data to be used as the basis for scientific planning so that physicians themselves, under the present system of the practice of medicine, will be better able to devise ways for equal and proper distribution of medical care to meet the health needs of all children in the post-war period; (2) to provide an armament of facts for intelligent argument against intervention by lay or government groups.

The study is by and for doctors of medicine. Practicing pediatricians are collecting the data. At the same time, the Academy expects govern-

ment agencies to accept the findings, since the United States Public Health Service will do all the manual statistical organization of the data submitted from the various states. (The Academy asked for and was granted advisory and statistical help from the Public Health Service and the Children's Bureau. These organizations enter the study only in those capacities.)

Encompassed by the study are an investigation of hospital facilities, public and semi-public health and community services; distribution, qualifications and activities of professional personnel; and the extent of pediatric education in the medical schools.

As their part, physicians in private practice are asked to fill out a one-page questionnaire, regardless of whether they see children in their practice or not. All information is strictly confidential.

Considering the scope and purpose of the study, this modest request appears to be one that should be complied with by even the busiest of physicians.

### **The Responsibility of the Physician in Premarital Examinations**

The premarital examination law was enacted in 1941, and has been favorably accepted by the public and the medical profession. During the war years, however, some abuses and some circumventions of the law appeared which have recently been made the subject of a study by the California State Board of Health.

The language of the law is, as laws go, remarkably simple. The law specifies merely that a physician shall give his opinion that "the person is not infected with syphilis, or if so infected, is not in a stage of that disease which is or may become communicable to the marital partner," and that a blood specimen, designated as a "premarital test" shall be submitted to a laboratory. How thorough an examination should be made is left by the law as an open question. The physician is asked only to sign a statement that the person is not infected with communicable syphilis.

The actual mechanism of taking care of candidates for marriage was purposefully made simple. The Premarital Act, as written, anticipated that the patient would go to his physician and thence to the laboratory with a request for a premarital test. The laboratory then returns its report to the physician on a special blank which the State De-

partment of Public Health has supplied the laboratory. If the test is negative the physician merely countersigns this report and gives it to the candidates for marriage, who in turn present it to the Marriage License Bureau.

It is, in fact, the very simplicity and minimizing of red tape which have allowed irregular practitioners and laymen operating laboratories to circumvent the original intention of the law. In the Los Angeles area, for instance, until the State Board of Health compelled their removal, several laboratories near the Hall of Records had large electric signs advertising "Marriage Examinations—Four-Hour Service," or equivalent.

It is self-evident that such advertising was not calculated to encourage the couples to seek out the physician of their choice as the law intended, but instead, as is the case with so many schemes to commercialize medicine, left the physician in the position of a sort of undesirable end-product who was useful only for his signature.

Recent questionnaire studies by the California State Board of Health on large numbers of couples who have had premarital examinations, reveal that in some areas as many as 40 to 50 per cent of these couples go directly to such lab-

oratories which advertise or which are under lay control.

These studies show public dissatisfaction with such abuses. On the contrary, the public is found to be well pleased with premarital examinations when they are administered well by qualified doctors. Almost invariably the answer to "Do you approve of premarital examinations," was "Yes." Under "Comments" many couples said these examinations were a good idea, but as administered were merely a "racket" or a "joke." Since the couples making such answers were the ones who had gone directly to advertising or lay laboratories, and had not seen a doctor at all, the answers were about what might have been expected.

All the patients who were given adequate examinations seemed well satisfied and did not complain of overcharges. Those patients who merely had their backs inspected for a rash sometimes complained that they had been "short-weighted." On the contrary, there were never any complaints that examinations were more thorough than needed. To quote the old professor's maxim, "A patient cannot himself ask the

doctor to remember to do a rectal examination."

It is unfortunate that the law requiring a three-day waiting period has now been abolished, for many couples tend to demand "Four-Hour Service" because they see it advertised. A bulletin of information is now being given to couples seeking a premarital examination by the California State Board of Health, which suggests that a three-day interval be allowed in order to permit an adequate time for the physician's examination and laboratory examination.

Entirely aside from financial gain or loss to the physician, the humanitarian aspect of the problem should appeal greatly as an opportunity for service. Marriage, even though the divorce rate in some communities now runs higher than 90 per cent, is still a not-to-be-forgotten time in an individual's life. Not only is this contact with people an opportunity for the physician to establish friendly relationships for the future, but the chance thus afforded to give of our counsel to these young couples may mean the difference between a happy married life and one ruined by ignorance or lack of understanding.

### **THE VETERANS' CHOICE**

Gratifying support for the medical profession came again last month from the American Legion, California Department. At its annual convention, with some 5,000 delegates present, the Legion adopted a resolution protesting compulsory health insurance and pointing toward the numerous voluntary medical care plans already available to the people of California.

Only last year the Legion went on record in this vein and participated in the fight against socialized medicine in the California Legislature. Now comes a reiteration of this stand, adopted not only by the guiding councils of the state Legion but by the entire slate of delegates. This comes from the rank and file itself and leaves no

doubt as to the position of the California Department of the Legion.

In the resolution opposing compulsory health insurance the Legion pointed out that such proposals "would increase the tax burden and would bring about regimentation of the medical profession." Left out of account was the fact that socialized medicine would lower the standards of medical care now received by Californians. We can only assume that the Legion regarded this topic as a scientific matter on which the doctors themselves are the best qualified observers. On the matter of regimentation, however, the doctors can think of no group better qualified to testify than the veterans of this country's two great wars.





## Clinical-Pathological Conference

### PRESENTATION OF CASE\*

White male, age 37. Occupation, Editor.

**History Summary:** The history of this patient's illness dates back to 1919, at which time the patient developed a severe and protracted diarrhea, characterized by 4 to 10 watery bowel movements daily, accompanied by blood and mucus. Initially the patient was not treated in this hospital. Treatment consisted of bismuth and opium with a working diagnosis of colitis on an allergic basis. as the patient had both hay fever and asthma clinically.

In 1929 a cecostomy was done because of continued rectal bleeding and a weight loss of severe grade, his weight at that time being 72 pounds. Following this the patient began to gain weight and the bloody diarrhea ceased, until two years later when the cecostomy began to close spontaneously and the bloody mucoid stools reappeared. The cecostomy was revised at this time with improvement of the patient.

From 1929 to 1937 the patient had been active and fairly comfortable. However, at the end of this time, pain was noticed at the cecostomy opening which increased gradually over the past four years until the present admission. He now complains of almost constant pain in this region with extreme soreness and hyperesthesia of the surrounding skin.

In May, 1941, the patient was admitted to the Los Angeles General Hospital, remaining for a two-month period. At this time the following findings were noted: Hb. 85 per cent, WBC 12,200, Polys 82 per cent, prothrombin normal. Barium enema per rectum revealed marked narrowing as far as the mid transverse colon beyond which the patient could not retain the enema. The mucosal pattern in the region outlined was almost completely obliterated. A barium enema given through the cecostomy opening demonstrated a narrow transverse and descending colon without normal markings, pipestem in character. There was considerable reflux into the terminal ileum. The patient was then dismissed with instructions to return in three weeks for further surgery. During this period the patient took exercises and sun baths with a weight gain to 116 pounds.

**Past History:** The usual childhood diseases. Severe cerebral concussion in 1939, without skull fracture. Tonsillectomy in childhood.

**Family History:** Not remarkable except that mother was subject to hay fever.

**Last Admission:** At the time of his last admission on August 7, 1941, the patient reported that small amounts of fecal material and mucus were discharged from the anus at monthly intervals. Physical examination on entry revealed a fairly well nourished white male in no acute distress.

Temperature 99.2, pulse 86, respiration 20, blood pressure 128/80. Head and neck not remarkable except for carious teeth. Chest, lungs and heart not remarkable. Abdomen showed a functional fecal fistula (cecostomy) but no tenderness, masses, rigidity, or hernia. Peristalsis was frequent and normal. The remainder of the physical examination was not remarkable.

**Laboratory Findings** (August 15, 1941): Hb. 88 per cent of 17 gms. RBC 5,090,000. WBC 9,800. Polys 72 per cent. Urine, essentially negative. Pothrombin 65 per cent. Wasserman on blood negative.

**Course:** The patient was prepared for ileostomy preliminary to colectomy. This included the placement of a Miller-Abbott tube which was seen by x-ray to have descended almost to the cecum.

**August 16, 1941:** A single barrel ileostomy was performed during which the terminal ileum was divided, the distal portion closed, and the proximal limb brought out. The postoperative course was uneventful. The ileostomy was permitted to drain on August 21st.

In December a notation is made that the patient had made little progress physically or mentally. He preferred lying in bed rather than getting up. He had several "mental breakdowns" and it was felt that rehabilitation was necessary, but after attempts at this were made, the rehabilitation service was forced to give up further efforts. During this time the following laboratory data was secured: October 18, 1941: Blood chlorides 512, calcium 10, phosphorus 4.2.

**January 18, 1942:** The patient began vomiting and the cecostomy became fiery red and swollen. There was no fecal drainage and the abdomen was markedly rigid. The ileostomy admitted the tip of the small finger. The temperature was 100 and pulse 130. Total proteins 7 gms. WBC 9,500, Polys 74 per cent, Hb. 68 per cent, RBC 3,900,000. An intestinal obstruction was feared and a Miller-Abbott tube was passed after an x-ray revealed several distended coils of intestine in the left abdomen. A film of the chest at this time revealed soft diffuse foci of infiltration scattered through both lungs, most profusely in the left, consistent with pneumonia. After passing the tube, x-ray showed the distended coils and the tube to be displaced to the left as if by an abdominal mass, although no mass was identifiable in the film.

**January 25, 1942:** X-ray showed the tip of the Miller-Abbott tube had passed to the lower abdomen and the previously distended loops of bowel appeared decompressed. At this time nodular densities were noted in both os innominata and the sacrum consistent with prostatic metastases. The left side of the body of the first lumbar vertebra showed marked destruction consistent with an osteolytic metastatic focus. At this time the patient showed a NPN 25, blood chlorides 656, and blood proteins 5.5 gms. total.

\* Taken from the Clinical-Pathological Conference, Seventy-fifth Annual Session of the California Medical Association, Los Angeles, May 7-10, 1946.

*February 8, 1942:* The patient now complained of severe occipital headache and pain in the spine. On rectal examination a mass was felt in the region of the prostate that was "not very firm and does not feel like normal prostate." The right Babinski was equivocal, the Gordon and Oppenheim were positive, and there was a spastic contracture of the right thigh with severe pain when moved. The left leg was normal. The tongue deviated to the left and difficult speech developed. The WBC was now 11,600, polys 72 per cent and Hb. 68 per cent. Despite the fact that the Miller-Abbott tube continued to function well (at one time actually emerging from the ileostomy), the abdominal distention persisted. Spinal puncture revealed a clear fluid with pressure of 175 mm. no cells, negative Wassermann and normal proteins. Barium instilled through the tube did not progress in 8 hours.

*February 17th:* The abdomen was said to be more distended but obstruction was not present as the ileostomy was functioning adequately. His condition seemed to be deteriorating rapidly and the patient expired February 18, 1942.—G.D.C.

#### DISCUSSION BY CLINICIAN

DR. J. HOMER WOOLSEY\*: The diagnostic problem that confronts us in this patient's history can be divided into two parts. In the onset he had obviously an ulcerative colitis of so-called undetermined origin. For it, we must comment, he had inadequate treatment, for any enterostomy in this disease should divert the fecal stream completely. The cecostomy that was done allowed the fecal stream to pass in part over into the diseased bowel and thereby keep the disease active. Eventually this cecostomy was revised.

The positive information given in this case history tells us that by barium enema there were marked pathological changes as high as the transverse colon. We should like the finding by rectal and proctoscopic study and also the bacteriological study of the rectal discharge. Not all but the majority of instances of true idiopathic ulcerative colitis arise in the rectum and gradually extend proximally.

We now come to the second part for diagnosis, since other symptoms not directly attributable to ulcerative colitis now arise. On August 16, 1941, an ileostomy was done. This means the abdominal cavity was exposed and information of value could have been obtained. In abdominal surgery a thorough examination of the viscera and recording of same should as a rule be done. Yet there are instances, and this is one, where such exploration could not be done, for even in the quiescent stage even slight handling traumatizes the bowel and may light up the disease or even rupture some of the friable bowel wall. Apparently no peritoneal tubercles or tumor metastases were observed.

The general course of the patient's illness is

now downward—loss of weight, strength, appetite and even interest to make any effort. By January, 1942, five months later, there was evidence of peritoneal irritation denoted by rigidity and vomiting, suggesting intestinal obstruction.

X-ray studies demonstrated a widely scattered pathology—changes in the pelvic bones indicative of metastatic carcinoma, a destruction of one side of the body of the first lumbar vertebra in contrast to involvement of the joint surface as would occur in tuberculosis and more likely in pyogenic osteomyelitis; changes in the lungs commensurate with congestion that could be metastases; and a displacement of the bowel into the left abdomen as if from a tumor mass and its associated adhesions with other viscera.

Later, nine days before death occurred, symptoms indicative of cranial involvement—headaches, changes in deeper reflexes of the right lower extremity; deviation of the tongue to the left and difficulty in speech, and a clear spinal fluid without cellular increase or protein change—were found.

Now, as I sum up the facts there existed an idiopathic, ulcerative colitis for 20 odd years. Mindful of the old precept that one disease with or without complications usually explains an illness, our thoughts are directed primarily to ulcerative colitis and its associated complications or sequelae.

Tuberculosis, however, must be strongly considered. We should have expected at the time the ileostomy was done some peritoneal tubercles or ileal involvement would have been noted; there would have been more involvement of the ileocecal region and less of the transverse and descending colon. The destructive process of the first lumbar vertebra is atypical of a tubercular lesion as previously mentioned. The pulmonary findings could represent a hematogenous extension, but again if tuberculosis was to be the main cause greater apical and hilar pulmonary involvement would be expected. The cranial metastases could occur but cellular change in the spinal fluid should have been present. Finally the rectal examination nine days before death occurred showed a mass on the rectal shelf above the prostate, that is in front of the colon, which would be associated with a peritoneal involvement, whereas if we were to have a tuberculous involvement we would have expected an extension down along the psoas muscle fascial plane from the involved vertebra and therefore would be behind the colon.

Abscess is common and hematogenous metastases of septic emboli giving osteomyelitis and lung abscess can occur. However, the metastases here are described as having characteristics otherwise than from an acute pyogenic type, and chills, fever, etc., of sepsis should have been prominent.

Malignancy in ulcerative colitis occurs in 2 per cent to 3 per cent of cases, is of the adeno type and arises from mucous membrane polyps that have occurred subsequent to the ulcerative colitis processes. There could have been a local involvement with local spread to have given a local

\* Woodland Clinic, Woodland.

tumor mass, displacing the bowel to the left, and also a metastatic mass palpated on the rectal shelf. A hematogenous spread with involvement of the lungs and the vertebra and the ilium is described by the x-ray studies. There was also some involvement of the nervous system in the brain stem region, having effect on the spinal motor tracts and the twelfth cranial nerve, for we are told of the disturbance in the deeper reflexes of the right lower extremity, of the deviation of the tongue to the left, and the difficulty in speech—apparently motor in origin.

It is my opinion, therefore, that this man had primarily an idiopathic ulcerative colitis and a sequela of carcinoma with local and distant metastases and death as a result of the carcinoma.

#### DISCUSSION BY PATHOLOGIST

DR. GILBERT CURTIS: We have had some very erudite discussions here this afternoon, and so far the pathologists have come off second best, if we were considering this to be a contest. Knowing the pathologists who were preparing the other cases, I thought I would go from the sublime to the completely ridiculous and make it so obvious that it might be missed. Dr. Woolsey has crossed me up completely in my attempt to get him out on some rare and unusual limb. The patient did have ulcerative colitis. He did have a malignancy. There was a rectal shelf; there was tumor in the vertebral bodies from top to bottom. We have to give Dr. Woolsey the palm.

Dr. Woolsey was worried whether the proximal portion of the large bowel had been investigated, but evidently he overlooked the fourth paragraph in the protocol, because this patient was given an enema through a very unusual stoma.

[Slide.] The film that you see on this lamp shows the enema per rectum. I thought it would be of interest to show you how small and contracted the lumen of the bowel may become. This is the rectum following up and across to the mid-transverse colon. That doesn't look like very much of a colon. Now, because they couldn't see the portion of bowel proximal to this region they did a further study.

[Slide.] This was an enema given through the cecostomy, and the large mass of barium that you see in the center of this picture is in the small bowel. If you look closely, you can also see, starting at about this point, the transverse and descending colon and down into the sigmoid have been outlined, showing you again that narrow little ribbon band spoken of as a pipstem colon. Without an illustration you would never recognize that as a colon.

[Slide.] It was noted later that difficulty had arisen in this patient's vertebrae. I would like to

put this film on to show you that they didn't miss this disease.

[Slide.] I put this film on to show you that when we first got him the vertebrae were normal. Because of the major difficulty that many of you no doubt have experienced in the passing of these Miller-Abbott tubes, I thought you would like to see one after it got out of your hand. Here we see many distended loops of small bowel with the tube in place. Numerous films were taken because it is felt that taking isolated spot films requires less work than doing radiography with a screen.

[Slide.] The findings in the chest film were very suggestive. I will put it on here for what it is worth. You can draw your own opinion as to whether you think that is compatible with metastasis or was just an ordinary bronchial pneumonia.

At the time of the autopsy no lung metastasis was found.

[Slide.] Now this film was somewhat of a surprise. Several months had elapsed since this patient was first seen in the hospital, and I must admit that, on the first film that was seen during his last entry, any change in the pelvic bones was missed.

[Slide.] This is a re-check with a much more efficient technique used, and you can see the typical moth-eaten appearance of the bone. It was both osteolytic and osteoplastic, portions of the bone being almost completely destroyed.

Subsequent films show almost the same findings.

[Slide.] This Kodachrome slide shows a specimen, an autopsy specimen, in this particular case, involving the entire colon. I thought you would like to see this because, although it is not at all unusual, there are many here who have not been through the autopsy department recently, and these lesions are so striking. I thought it would be well to show the surgeons just exactly what they are up against when they have this type of patient.

You notice that this bowel shows many areas of polyp formation. These polyps are particularly numerous in the descending portion of the colon.

This man's initial malignant lesion was very insignificant. It had penetrated the wall of the bowel, rather than forming any bulky mass in the lumen of the bowel, with very extensive peritoneal metastasis.

I would like to show you a blown up portion of this area, which gives you a bit of an idea of how this bowel appears in the gross.

[Slide.] We have thickening and deep and shallow ulceration. The ulcers may be right through to the peritoneum and as a result, the patient may expire following colectomy because the surgeon may put his finger through one of these ulcers. This specimen happens to be from that type of complication.





## CLINICAL CONFERENCE

FROM THE LOS ANGELES COUNTY GENERAL HOSPITAL SERVICE OF THE UNIVERSITY OF SOUTHERN CALIFORNIA SCHOOL OF MEDICINE

DOCTOR CLARENCE J. BERNE:\* The patient to be considered today has a common disease with a few unusual features. Important problems in this type of case are being dealt with daily by many general surgeons. Doctor Blatherwick will present the case history.

*Presentation of the Case* by the Resident, Doctor Norman Blatherwick:

This 21-year-old white housewife entered the hospital because of attacks of pain in the right upper quadrant of the abdomen.

Three months ago she was delivered of a full term child. The pregnancy and delivery were normal. Soon afterward, the attacks of sudden severe pain began, frequently after a fatty meal. The pain was located along the right costal margin and radiated to the angle of the scapula on the same side. Nausea and vomiting accompanied the attacks. There was intolerance to fatty foods. The family physician had seen her in several attacks, and he had given morphine with relief of pain. She stated that possibly on one occasion the stools were light and the urine dark after an attack. Jaundice was denied. However, at the time of her first visit to the out-patient clinic one week before admission, there was mild but definite jaundice. The past medical and family histories were otherwise uninformative. She had taken no hepatotoxic medication.

Physical examination revealed a well nourished young woman of the sthenic type. No icterus could be made out. The physical findings were all quite normal. Particularly, the liver, spleen and right kidney could not be felt and there was no tenderness in the upper abdomen. The temperature, pulse and respirations were normal. The blood pressure was 108 mm. of mercury systolic, 70 mm. of mercury diastolic. The hemoglobin was 90 per cent and the leucocyte count 9,250 per cu. mm. with 75 per cent neutrophils. No abnormalities were found in the urine. Serologic tests for syphilis were negative. The icteric index was 7 units two days following admission and 11 units a few days later. The blood prothrombin determination was normal. The blood cholesterol was 235 mg. per 100 cc. The serum albumin was recorded as 4.2 gm. and the serum globulin as 1.2 gm. per 100 cc.

DOCTOR BERNE: We will ask Doctor Pattison to discuss the diagnosis on the basis of the record up to this point.

DOCTOR ARTHUR C. PATTISON:\* The history of this patient's disease breaks down readily into two phases: the first is of pain characteristic of biliary colic associated with qualitative dyspepsia between attacks, the second is the appearance of jaundice. Although attacks of biliary colic may occur without calculi being present, the appearance of jaundice makes it necessary to conclude that common duct involvement has occurred, and the most likely explanation is that one or more calculi have entered the common duct. When the clinical picture is correlated with the recent pregnancy, one of the most important known etiologic factors in cholelithiasis is added. The manner in which pregnancy influences the development of gall stones is not known, but it is probably involved with cholesterol metabolism more than it is related to stasis. Because this patient's description of her pain is so typical of biliary colic, and because of the secondary appearance of transient jaundice, I believe that a diagnosis of cholelithiasis is justified.

Cholelithiasis in the young may be conditioned by another factor, the excessive excretion of bilirubin seen in the presence of familial hemolytic icterus. There is no familial history of jaundice in this patient, no attacks of jaundice preceded the attacks of pain, and there is no anemia. Further blood studies, including erythrocyte fragility tests, would be necessary to exclude such a possibility completely. Other lesions capable of producing the syndrome presented by this patient may now be considered. It could result from a duodenal ulcer located low in the second portion of the duodenum, and involving the papilla of Vater. Inflammation in a peri-Vaterian duodenal diverticulum could produce such a picture. Both lesions are quite rare, however, and an upper gastro-intestinal x-ray study would be necessary to establish such diagnoses. We have seen instances of pseudobiliary colic in cirrhosis of the liver which have closely simulated biliary colic. Although the jaundice would be consistent with cirrhosis, the history, physical findings and laboratory studies in this case all fail to suggest the presence of cirrhosis.

Renal colic may closely resemble biliary colic, but the bedside differentiation at the time of an attack usually is not difficult; of course, at this time the presence of jaundice is a deciding factor in favor of the biliary tract lesion. Jaundice may

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occur secondary to pyelonephritis, presumably as the result of a secondary hepatitis, but is quite rare. A much greater problem in young people is the differentiation between obstruction of the common duct and primary hepatitis, particularly the infectious hepatitis due to virus infection (formerly called catarrhal jaundice). The sporadic atypical case of infectious hepatitis may, like syphilis of the liver, simulate many lesions of the biliary tract and must be diagnosed laboriously by exclusion, and waiting. Fortunately vitamin K has made the waiting much safer. In this case the intensity of the pain, and its occurrence dissociated from the jaundice would reasonably exclude infectious hepatitis, and the same may be said for toxic hepatic injury. One might ask whether or not there is enough evidence of liver disease to make us call upon the laboratory for more help. It seems that there is not. It becomes apparent that our differential diagnosis has presented no other condition that seems likely.

Consideration should next be given to the x-ray studies. They will be reported by Doctor Blatherwick and discussed by Doctor Berne.

DOCTOR BLATHERWICK: The gall bladder is well visualized, its size and position are normal for the patient's habitus; there are no filling defects, and there is good emptying after the fat meal.

DOCTOR BERNE: In cases with clinical pictures similar to this a presumptive diagnosis of gall bladder disease with calculi would be arrived at by most clinicians. The difficulty is the presence of a normal cholecystogram. With this diagnostic procedure false-positive tests are the most common error, and the cause usually can be identified by a check on the factors of assimilation, liver function and radiologic technique. Priodax has been a significant contribution to the reduction in the size of this false-positive group. A false-negative test, however, must usually be checked entirely on clinical grounds. Two important conditions in which false-negative tests occur are cholesterosis of the gall bladder and the cholelithiasis of the parturient primipara. In the latter instance it is usual for the calculi to be millet sized, not numerous, and be contained in a gall bladder otherwise normal. The same situation can occur, of course, at other ages and in the opposite sex, but it is particularly likely in women of this patient's status. The usual radiologic technique may show a normal gall bladder and no calculi. But if the film be made with the patient standing, enough calculi may gravitate and pile up in the fundus to enable their detection. Awareness of this fact may, if coupled with a strong clinical conviction, furnish the clinician a basis for securing such films. Further, if the upright films are negative, one must be prepared, under such circumstances, to advise operation. In this case we have such a situation and surgical treatment is therefore advised.

There exists a second consideration of importance; the "yellow flag" has been raised. It, therefore, becomes mandatory to assume that a common

duct lesion, almost certainly a calculus, does exist or has existed. When jaundice occurs as the result of gall stones, it must be assumed that the common duct is involved. This patient's common duct must be explored at the time of surgery. Negative palpation will not alter this responsibility. Surgery for gall stones is biliary tract surgery, not gall bladder surgery. Many of the most experienced surgeons now open the common duct on nearly half their cases of cholecystectomy and find stones in half the ducts so explored. Every surgeon who operates for gall bladder disease must be keenly aware of the indications for choledochotomy. It has been said that the bug-bear of gastroenterostomy is jejunal ulcer; it might also be said that the bug-bear of cholecystectomy is the overlooked common duct stone. Such a stone may not produce jaundice until the patient has recovered from a cholecystectomy.

Such principles must be applied in the case we have today. It might be argued that further observation or studies are indicated. Waiting will invite complications. This patient's situation is so typical that in our opinion it is wisest to make the diagnosis of cholelithiasis on clinical grounds and advise surgery.

Relative to the surgical treatment of cholelithiasis much can be heard regarding poor results. One of the potent causes of poor results is procrastination. Between attacks the patient may be well. Both the patient and the doctor may gamble on avoiding recurrence. We must realize that once stone migration is attempted, the process is basically progressive. With progression, complications develop. These may involve the liver, the ducts, and the pancreas as well as the gall bladder. The more extensive the involvement becomes, the less reversible is the process. Ideal results are most possible if surgery can be done before complications have developed, and therefore surgery is clearly indicated when attempted migration has been diagnosed.

Another important factor in determining poor results is the failure to do a complete and meticulous exploration of the entire abdomen including the esophageal hiatus area as soon as the abdomen is opened. The resultant failure to detect co-existing undiagnosed lesions often results in their effects being attributed to failure of the biliary tract surgery. A third group of poor results are dependent upon technical accidents at the time of cholecystectomy, conditioned by the presence of severe pathologic change or the presence of anomalies. In regard to the anomalies, it is a rare surgeon who can remember them all. Every case should be approached as though it presented an unknown anatomical arrangement and nothing should be clamped or cut or tied until it has been positively identified.

One other phase of treatment may be mentioned as it applied to this case. Exploration of the choledochus will require that drainage of it be established with a T-tube. Before removal of the tube, cholangiography will be done by the injection of lipiodol down the tube under fluoro-

scopic observation. Nitroglycerin will be given sublingually just before the injection. Free flow into the duodenum, with no filling defects in the duct, will give assurance that removal of the tube can be safely carried out. If a calculus is found, having been undetected at the time of surgery, we will resort to Best's regime. If that fails, Pribram's method of ether injection may be cautiously tried. If the calculus is still not dislodged reoperation will be postponed for some time and the Best regime will be repeated frequently.

#### FOLLOW UP NOTE

At the time of operation the gall bladder was found to be grossly normal. It contained about 20 calculi the size of wheat grains. One 5 mm. stone was present in the common duct. Microscopic study of the gall bladder wall revealed subserosal thickening and round cell infiltration of the mucosa. The convalescence was satisfactory. Cholangiogram was negative. Six weeks after discharge the patient was seen in out-clinic and was free of her previous symptoms.

### ARMY PHYSICIAN FINDS PENICILLIN EFFECTIVE FOR SORE THROAT

After studying 28 soldier-patients in the Hawaiian Islands, Capt. Selvan Davison, Medical Corps, Army of the United States, concludes that penicillin has a definite place in the treatment of acute sore throat.

Writing in the July 27 issue of *The Journal of the American Medical Association*, Captain Davison says that while penicillin gave good results in all of the acute sore throat cases which he treated, it was found especially effective in patients whose illness was due to the germ called hemolytic streptococcus. This germ is implicated in a large number of acute sore throat cases.

Captain Davison states that he undertook his study because doctors forever are seeking an ideal therapeutic measure which will obtain rapid and complete cure for sore throat.

The army physician quotes one investigator who previously had treated 28 cases of acute sore throat with penicillin, using 15,000 units every four hours, day and night. In this study, it was found that cases treated for less than six days with 15,000 unit dosages of penicillin showed comparatively poor results because of frequent relapses; yet patients treated for six full days showed excellent results.

Captain Davison says that on the basis of the previous investigation, he studied the possibility of giving a shorter but more intensive course of penicillin treatment.

All of Captain Davison's patients were young adults with no complicating diseases. No patients were treated who had been ill for more than 48 hours.

Penicillin was administered in the amount of 20,000 units every three hours, day and night, by intramuscular injection. The average total dosage of penicillin was 360,000 units over a period of 54 hours.

There was only one relapse, in which recovery occurred without further penicillin. One case did not respond until sulfadiazine replaced penicillin as the treatment.

Most of the patients showed complete recovery in two or three days. The patients from whom no bacteria were obtained displayed normal throats in an average of under four days.

"It must be remembered," Captain Davison writes, "that the periods of time noted are the upper limits. Disappearance of symptoms and of signs means complete absence. There had to be not the slightest pain on swallowing nor any remaining exudate or inflammation before a time element was established."



# MEDICAL PROGRESS

## THE Rh FACTOR IN CLINICAL OBSTETRICS

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OBSTETRICIANS have recognized with extraordinary rapidity the practical importance of the recently-gained knowledge concerning the Rh blood factor. Since its discovery by Landsteiner and Wiener<sup>5</sup> in 1940, the clinical implications of its behavior have been accorded widespread consideration and use. Indeed, the mechanism of action of the Rh factor both in transfusion reactions and during gestation is now such common knowledge, thanks to numerous comprehensive review papers,<sup>2,3,11,14,15</sup> that more than a brief recapitulation here of the basic facts would be redundant.

Approximately 85 per cent of individuals of the white race carry in or on their red blood cells an antigen known as the Rh factor—they are "Rh-positive." The remaining 15 per cent are Rh-negative in that they do not possess this antigen. When Rh-positive red blood cells are introduced into the tissues or blood stream of an Rh-negative individual, the serum of the latter may develop Rh antibodies which have the power of agglutinating and/or hemolyzing Rh-positive red blood cells. This antibody-producing ability varies considerably among Rh-negative individuals, sensitivity to the antigen being high in some and quite low in others. Such iso-immunization or sensitization, once established, may persist for long periods of time.

This mechanism explains many of the transfusion reactions which occur between apparently compatible bloods; the latter are compatible in the A, B, O group system but not for the Rh characteristic. Such transfusion reactions occur in individuals who have been immunized to Rh-positive red blood cells by previous transfusion, multiple transfusions, intramuscular injection of blood, or by iso-immunization attendant on gestation. The latter is of especial interest to the obstetrician.

The possession of the Rh factor by the red cells of an individual is a matter of inheritance. The characteristic is brought about by two allelic genes represented as Rh (positive) and rh (negative), the former being a dominant gene in the Mendelian sense. Thus an Rh-positive phenotype may be either homozygous (RhRh) or heterozygous (Rhrh), whereas an Rh-negative phenotype can only be homozygous (rhrh). It is apparent, then that any mating involving a homozygous Rh-positive husband or wife can only give rise to an Rh-positive phenotype offspring. Where both husband and wife are Rh-negative the child must also be Rh-negative.

The obstetrician is especially concerned with those matings in which the wife is Rh-negative and the husband Rh-positive, for if the latter be homozygous an Rh-positive child will always result, while if he be heterozygous there is a 50 per cent chance of producing an Rh-positive child. It is when this type of Rh mismatching occurs—an Rh-positive child borne by an Rh-negative mother—that

that serious obstetrical problems are most likely to eventuate. The chance that such a mating will result in an Rh-positive child is about 70 per cent.

Under these circumstances the presence of the Rh-positive child in utero may lead to iso-immunization of the mother. The basic mechanism responsible for this effect is probably the introduction of fetal red blood cells into the maternal circulation, but the factors controlling its occurrence and extent remain to be clarified. A defect in the placental barrier must be postulated; and it may be that the not uncommon "deportation of villi" satisfies this requirement. The known variability of sensitivity to Rh antigen action undoubtedly plays some part in the maternal reaction to fetal red blood cells. In any event, many Rh-negative mothers who carry Rh-positive pregnancies show no evidence of Rh antibody formation, whereas others develop a rapidly rising titer.

Whatever the regulatory factors may be, whenever an Rh-positive fetus immunizes an Rh-negative mother the maternal antibodies are passed through the placenta to the fetus with varying detrimental results to it. There is thus produced an agglutination and hemolysis of the fetal Rh-positive red blood cells, resulting secondarily in progressive anemia, liver damage, splenomegaly, hypoproteinemia, jaundice, edema, extramedullary erythropoiesis, placental changes, and fetal hypoxemia; in short, all the signs of erythroblastosis fetalis. This is, indeed, the generally accepted pathogenesis of the major percentage of cases of this disease—perhaps better termed hemolytic disease of the newborn.

This mechanism may function with varying speed in different Rh-negative mothers; rapid production of maternal antibodies with severe damage to the fetus may occur in the first pregnancy of one mother; iso-immunization in another mother may not become well enough established to be appreciably harmful to the fetus until the second, third, or fourth pregnancy.

Transfusion of incompatible Rh blood, however, constitutes a more direct method of establishing Rh antibodies in an Rh-negative mother—without the occurrence, be it noted, of any transfusion reaction. Giving such a woman Rh-positive blood—at any time prior to or during the childbearing age—may establish such a potentially high level of Rh antibodies that the Rh-positive infant of a subsequent pregnancy, subject to the hemolyzing and agglutinating action, may manifest hemolytic disease of the newborn.

The foregoing summary of the role of the Rh factor in the etiology of hemolytic disease of the newborn (erythroblastosis fetalis) is, of course, an oversimplification, for many cases of the disease—to be discussed presently—cannot be accounted for on this basis. Perhaps a scrutiny of clinical cases will point out more clearly the areas of the Rh-factor problem where our knowledge is incomplete.

### INCIDENCE OF HEMOLYTIC DISEASE OF THE NEWBORN

In its full-blown manifestation erythroblastosis fetalis presents an unmistakable clinical picture,

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whether in the icterus gravis or hydrops fetalis variety; and even lesser degrees of hemolytic disease of the newborn leave little doubt as to the diagnosis. But a moderate number of newborn infants in whom a definite diagnosis of erythroblastosis cannot be made show, nevertheless, one or more of the physical signs and laboratory findings associated with the disease. The incidence of such offspring in matings involving mixed Rh types has been such as to lead us to feel that we may be dealing with subclinical manifestations of hemolytic disease of the newborn. (Indeed, the occurrence of such cases constitutes one reason for preferring the broader term "hemolytic disease of the newborn" to the narrower one "erythroblastosis fetalis.")

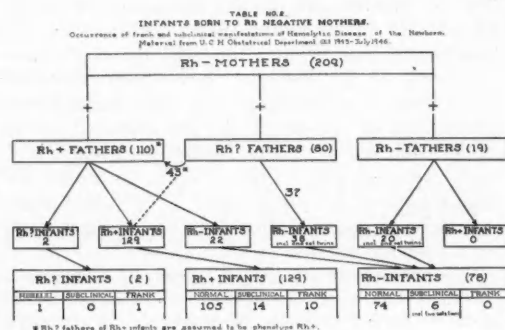
Thus, the occurrence of such conditions as enlarged liver, enlarged spleen, nucleated red blood cells in excess of 5 per 100 white blood cells, icterus, bleeding tendencies, anemias, golden yellow amniotic fluid, hydrocephalus, and edema may well be evidences of a mild trauma to the fetus resulting from Rh iso-immunization. From the series of cases to be presented here we have selected 20 which seem to warrant consideration from this point of view. The clinical bases for this selection are presented in Table No. 1. In considering the obstetrical aspects of the Rh factor it is well to bear in mind that these subclinical

TABLE 1.—Findings in Infants Judged to Show Subclinical Manifestations of Hemolytic Disease of the Newborn (20 cases)

Rh POSITIVE INFANTS:	
* Case No. 1:	Icterus, enlarged spleen, NRBCs—4%
No. 2:	Persistently enlarged spleen
No. 3:	Persistently enlarged liver and spleen
No. 4:	NRBCs—14%
No. 5:	Persistently enlarged liver and spleen
No. 6:	Yellow vernix, enlarged liver and spleen, NRBCs—12%
* No. 7:	Prematurity, icterus, anemia, enlarged liver, NRBCs—9%
No. 8:	Icterus, enlarged liver and spleen, NRBCs—10%
No. 9:	Persistently enlarged liver and spleen, Melena
* No. 10:	Edema, icterus, NRBCs—4%
No. 11:	Enlarged spleen, NRBCs—6%
No. 12:	Enlarged liver, icterus, petechiae, NRBCs—4.5%
No. 13:	Yellow amniotic fluid, enlarged liver
No. 14:	Prematurity, enlarged spleen, hydrocephalus, NRBCs—1%
Rh NEGATIVE INFANTS:	
No. 15:	Icterus, enlarged liver and spleen, NRBCs—5%
No. 16:	Icterus, enlarged liver, NRBCs—4%
No. 17:	Enlarged liver, NRBCs—5%
No. 18:	Enlarged liver, persistent edema
* No. 19:	Icterus, anemia, enlarged spleen, NRBCs—40%
No. 20:	Icterus, NRBCs—8%
* Cases in which a diagnosis of hemolytic disease of the newborn was entertained but not definitely made.	
("NRBCs—10%" signifies "nucleated" red blood cells—10 per hundred WBCs.)	

cases may well represent a group of infants with an impaired but not hopeless survival prognosis, a group which will be the most susceptible to salvage through clinical alertness and skillful therapy.

The very nature of Rh iso-immunization indicates that from a practical clinical viewpoint the pregnancies of Rh-negative mothers will require the principal attention. The illustrative material here presented consists of 209 such pregnancies resulting in the birth of 211 infants (two sets of twins) in the Division of Obstetrics and Gynecology of the University of California Hospital. Table No. 2 presents the data concerning them with regard to: Rh factors involved in each mat-



ing, Rh status of the infants, and presence or absence of hemolytic disease of the newborn.

Table No. 3 presents the incidence of hemolytic disease of the newborn for the 209 pregnancies. There were 11 frankly erythroblastic babies, an incidence of 5 per cent. Of these 11 infants only two survived, a mortality of 82 per cent. Twenty infants of these pregnancies showed subclinical manifestations of hemolytic disease of the newborn, an incidence of 10 per cent. All of these 20

TABLE NO. 3  
INCIDENCE OF HEMOLYTIC DISEASE OF THE NEWBORN IN INFANTS OF Rh NEGATIVE MOTHERS. (211 INFANTS)

TOTAL INCIDENCE	FRANK—	5.2% (11)	14.7%
	SUBCLINICAL—	9.5% (20)	
INCIDENCE IN Rh+ INFANTS	FRANK—	5.2% (11)	11.8%
	SUBCLINICAL—	6.6% (14)	
INCIDENCE IN Rh- INFANTS	FRANK—	0% (0)	2.9%
	SUBCLINICAL—	2.9% (6)	

infants survived the neonatal period. Fifteen per cent, then, of infants of Rh-negative mothers suffered from the effects of iso-immunization, and for these 31 infants the mortality was 29 per cent.

#### RELATION OF HEMOLYTIC DISEASE OF THE NEWBORN TO PARITY

All investigators have emphasized that increasing parity subjects successive Rh-positive infants to increasing risk. But there has been, perhaps, an overemphasis on the degree of safety enjoyed by the child of a primigravida mother. While our series of cases is too small to permit full analysis with regard to parity of the mothers, an inspection of it from this viewpoint is illuminating. Of the 211 infants 92, or 44 per cent, were delivered of primigravidae. Of the 31 cases of



hemolytic disease of the newborn 12, or 39 per cent, were infants of primigravida pregnancies, and of this number 2 were cases of frank erythroblastosis fetalis. It is apparent, then, that when a mother is Rh-negative obstetrical vigilance cannot be relaxed appreciably simply because she is carrying her first pregnancy.

#### ANTEPARTUM PREDICTION OF HEMOLYTIC DISEASE OF THE NEWBORN

What observations shall this vigilance include? Fortunately, the availability of fairly simple and satisfactory titration methods,<sup>15</sup> not only for Rh typing but also for Rh antibodies, provides an opportunity to be forewarned prior to delivery of an infant with hemolytic disease of the newborn. Rh typing of all pregnant mothers at once separates them into an Rh-positive group, in which the likelihood of fetal affliction is extremely small, and an Rh-negative group in which its incidence is high. When, in the latter group, the father is Rh-positive, continued attempts must be made to discern the presence of the disease in the intrauterine fetus.

This is best—though still unsatisfactorily—accomplished at present by means of repeated antepartum determinations of maternal Rh antibody titer. While the interpretation of titer levels is not yet clear, most workers agree that the appearance of any detectable Rh antibody in the maternal serum should warn the obstetrician that the intrauterine fetus is probably being subjected to hemolytic disease damage.

Fig. 1 presents a graphic representation of the correlation, for our series of cases, of the clinical status of infants of Rh-negative mothers and

here they have been consolidated to absent, trace, and present.

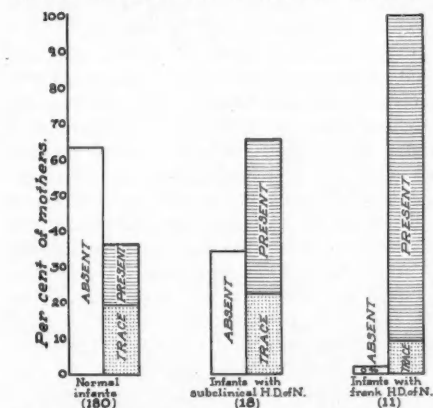
One hundred per cent of mothers of frankly erythroblastotic infants showed the presence of a trace or more of Rh antibodies. Sixty-six per cent of the mothers of infants with subclinical hemolytic disease of the newborn showed a trace or more—though 34 per cent of such mothers showed no titer at any time even though their infants apparently suffered from some degree of the disease. Sixty-four per cent of the mothers of clinically normal infants showed no Rh antibody. Note, however, that 36 per cent of such mothers did develop antibodies even though no evidence of iso-immunization damage could be clinically observed in their infants. The cause of such antibody development is at present unknown—or, from the opposite viewpoint, the reason why the babies are protected from damage is unknown.

From a clinical point of view we can only conclude that while the antepartum occurrence of maternal Rh antibodies leads to an increased expectancy of delivery of a damaged infant, it does not necessarily predict such an outcome. On the other hand, absence of maternal Rh antibodies does not necessarily mean that the infant will escape all manifestations of hemolytic disease of the newborn—though in the small series reported here frank erythroblastosis was invariably associated with the development of maternal Rh antibodies (only a trace in one case).

The recent discovery by Wiener<sup>15,16</sup> of the so-called "blocking antibody" has complicated the situation. While the exact nature of this antibody is as yet undetermined, it is known to act in such a way as to spoil or "block" the usual agglutination test for Rh antibodies. Thus, the presence of blocking antibodies in maternal serum may serve to obscure the presence of Rh agglutinins if only the simple test for the latter is run. Fortunately, the blocking antibodies may be titrated separately;<sup>16</sup> and it is likely that both tests will be required for all antepartum mothers where Rh immunization is suspected if we are to predict with any accuracy the occurrence of hemolytic disease of the newborn. The findings represented by Fig. 1, for example, are probably explained to some extent by the blocking antibody factor, which was not taken into account in this analysis.

Recently, however, Page, Hunt, and Lucia,<sup>9</sup> testing antepartum maternal sera for both Rh agglutinins and blocking antibodies, have given further insight into the significance of these antepartum titrations. Their findings indicate that while the height of the titer may tell us something about the likelihood of hemolytic disease of the newborn, much more indicative is the *length of time* before delivery that these antibodies are present in maternal serum. The graphic chart of Fig. 2 was constructed, with the permission of the authors, from the data of Page, Hunt and Lucia's paper. (Their clinical criteria for subclinical manifestations of hemolytic disease of the newborn approximate our own.)

RELATION OF MATERNAL ANTI-RH ANTIBODIES TO THE CLINICAL STATUS OF INFANTS OF RH NEGATIVE MOTHERS.



Percent of mothers of each group of infants showing presence or absence of anti-Rh antibodies at any time during pregnancy or puerperium. (Twins considered as one infant.) (Trace of antibody equals less than 1-plus titer.)

Fig. 1.

the presence or absence of maternal anti-Rh titer at any time during pregnancy or the puerperium. In the 209 pregnancies titers were recorded as absent, trace, 1-, 2-, 3-, and 4-plus; for analysis

RELATION OF INCIDENCE AND DEGREE OF FETAL MANIFESTATION OF HEMOLYTIC DISEASE OF THE NEWBORN TO ANTEPARTUM DURATION OF THE PRESENCE OF MATERNAL ANTI-Rh ANTIBODIES  
(Data from Page, Hurst and Lucia: in press.)

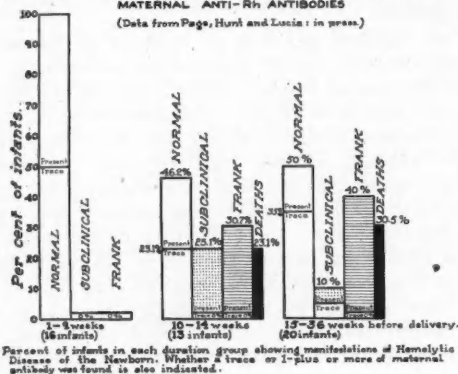


Fig. 2.

While their series of cases is small, it is highly suggestive of certain conclusions. When either antibody appeared in the maternal serum only 1 to 9 weeks before delivery, 100 per cent of the delivered infants were clinically normal. When it appeared 10 to 14 weeks before delivery, 54 per cent of the delivered infants showed some evidence of hemolytic disease of the newborn. When it appeared 15 to 36 weeks before delivery, 50 per cent of infants showed the disease.

More important than incidence of the disease is the fact that the severity of its manifestation paralleled even more closely the antepartum duration of maternal titer. Thus, in the 1- to 9-week group there was no frank erythroblastosis fetalis; in the 10- to 14-week group 31 per cent of the infants had frank erythroblastosis fetalis, and the mortality for the group was 23 per cent; in the 15- to 36-week group 40 per cent of the infants were frankly erythroblastotic, and the mortality for the group was 31 per cent.

The clinical implications of these findings are so clear-cut that reference will be made to them again in the discussion of prophylaxis and treatment of hemolytic disease of the newborn.

#### HEMOLYTIC DISEASE OF THE NEWBORN FROM CAUSES OTHER THAN Rh IMMUNIZATION

Table No. 3 shows an incidence of 3 per cent of hemolytic disease of the newborn occurring in Rh-negative infants, all of the 6 cases thus represented being subclinical manifestations. But that frank erythroblastosis fetalis may occur under similar circumstances is illustrated by the case of a private patient not included in our series. This patient was a 21-year-old primigravida whose blood study revealed a negative Kahn and Kolmer, Group O, Rh-negative. The delivered infant, Group A, Rh-negative, had frank erythroblastosis fetalis but survived the neonatal period. Postpartum study of the maternal serum showed no evidence of Rh antibodies but the anti-A titer fluctuated between 1/128 and 1/1024. Boorman, Dodd and Mollison<sup>1</sup> reported two cases of clini-

cal erythroblastosis fetalis in infants whose bloods were both Group B, Rh-positive while those of the mothers were Group O, Rh-positive. The maternal anti-B titers were 1/3200 and 1/8,000,000 respectively. LaVake<sup>6</sup> reported a similar case. Polayes<sup>10</sup> reported two cases of Group O, Rh-positive mothers who bore Group A, Rh-positive infants; both infants were frankly erythroblastotic. The maternal anti-A titers were 1/700 and 1/750 respectively.

It is clear then that iso-immunization by antigens other than the Rh antigen may, through a similar mechanism, produce hemolytic disease of the newborn. Indeed, it is likely that Rh subgroup reactions may account for a few cases, eight such sub-groups having been established.<sup>15</sup> The part that M, N, and P sub-groups may play has not yet been delineated.

The existence of an Hr antigen has also been established,<sup>7,8,13</sup> so called because it is present in the blood of Rh-negative individuals. While it appears to have been the etiological factor in a few cases of hemolytic disease of the newborn, its importance has not yet been clarified. At present, however, titrations of it are thought to be of some value in determining whether an Rh-positive individual is homozygous or heterozygous, a matter of considerable importance in predicting the status of future infants of Rh-positive father-Rh-negative mother matings.

On the whole, however, obstetricians will be well advised to bear in mind that hemolytic disease of the newborn may occur unexpectedly, though very rarely, in infants of matings where the bloods are supposedly compatible.

#### PROPHYLAXIS OF HEMOLYTIC DISEASE OF THE NEWBORN

Protection of prospective mothers from iso-immunization, insofar as this is possible, is, of course, of prime importance in preventing the occurrence of hemolytic disease of the newborn. Any woman before or during the childbearing age for whom blood transfusion is contemplated should have Rh typing as well as the routine cross-matching procedures in order to eliminate the possibility of introducing Rh-positive blood into an Rh-negative blood stream. Obstetricians and pediatricians cling to the habit of giving blood intramuscularly to newborn infants for various purposes. Whether an iso-immunization to the Rh factor thus produced in a female child would persist long enough to increase the fetal hazard in a subsequent pregnancy has not yet been established; but until enough years pass to clarify this point it might be advisable to avoid this time-honored but dubious procedure.

That all pregnant women should routinely have Rh typing is self-evident. The husbands of those who are Rh-negative should be similarly studied in order to prepare for and warn the prospective parents of the possible eventualities. While the present serological methods for determining whether an Rh-positive father is homozygous or

heterozygous are still in the experimental stage, we may reasonably expect them to be developed to a degree of dependability which will make the prediction of the chances for the occurrence of an Rh-positive child much more certain. For the present, careful scrutiny of the previous obstetrical history in multigravidae often constitutes the only mode of approach to this information.

Dissemination of information about the Rh factor and erythroblastosis through lay publication channels has resulted in the obstetrician being increasingly confronted by requests for advice from worried prospective parents—especially when the latter have discovered that they are Rh incompatible. Even nulliparous wives now express doubts about undertaking pregnancy at all in the face of such incompatibility.

Such patients may be reassured by the fact that the likelihood of a primigravida mother bearing a frankly erythroblastotic child is not great, and that even if one is borne its survival chances are reasonably good. Potter and Wilson,<sup>12</sup> reporting over 100 erythroblastotic infants, found 100 per cent survival in those borne by primigravidae—though the number of such infants is not given. (Indeed, this absence of mortality for an admittedly lethal disease leads one to wonder about their criteria for diagnosis.) On the other hand, the likelihood that an Rh-negative mother with an Rh-positive husband will bear a frankly erythroblastotic child is not as negligible as some authors have suggested. Even in our small series two such cases were encountered, neither one of which was the result of previous transfusion, and only one of which survived. The primigravida, however, runs such a small risk of bearing a still-born or seriously injured infant that when she allows fears about erythroblastosis to upset her, emphasis should be placed on the probability of a happy fetal outcome.

The outlook for the later pregnancies of the Rh-incompatible couple is less hopeful though not by any means grave. If, in previous pregnancies, no serological or fetal clinical evidence of maternal iso-immunization has been encountered, the risk to the child is not much greater than it was in previous pregnancies, and the patient may be reassured on this basis.

Once maternal iso-immunization has been established, however, the picture changes abruptly. In subsequent pregnancies the likelihood of an unfortunate fetal outcome greatly and progressively increases—especially if the father be a homozygous Rh-positive. Guidance of the iso-immunized mother constitutes a difficult problem. Our knowledge of the factors involved in the production of hemolytic disease of the newborn is still too incomplete to permit of any definitive decision regarding advice to mothers under such circumstances. Cases will require individualization based on serological study and previous obstetrical history. But with increasing frequency three questions present themselves: that of the justification

for sterilization, the justification for therapeutic abortion, and the propriety of artificial insemination with semen from an Rh-negative donor. The final answers become a matter for individual decision, to the ease of which further knowledge will undoubtedly contribute.

The study of antepartum anti-Rh and blocking antibody titers, however, offers one avenue of attack in the prophylaxis of hemolytic disease of the newborn. Dependence upon the level of titer alone would seem ill-advised at present. Uncertainty still exists regarding its significance. A rising titer may indicate increasing damage to the fetus or it may not. Possibly a rising titer followed by a fall may point to more rapid absorption of maternal Rh antibodies by the fetus with consequent increasing damage.<sup>4</sup>

The work of Page, Hunt, and Lucia, however, suggests very strongly that the antepartum duration of detectable maternal anti-Rh (or blocking antibody) titer may serve as a measure of the severity of hemolytic disease in the intrauterine fetus. Present opinion is divided on the value of premature interruption of pregnancy for the purpose of averting serious manifestations of the disease in the newborn. It is difficult to decide between the increasing hazards which go with increasing prematurity and those to which a fetus is subject while it remains in an environment where Rh antibodies have access to its blood.

On the other hand, if the findings of Page, Hunt and Lucia are confirmed by larger series it would appear that increasing time spent by a fetus in such a detrimental uterine environment—no matter what the type and concentration of maternal Rh antibodies—is more damaging than we had suspected. The dividing line between serious and subclinical damage would seem to fall at approximately 10 weeks antepartum. For an Rh-negative mother, then, who first evidences anti-Rh titer *less than 10 weeks* before term it would seem advisable to allow spontaneous onset of labor unless the pregnancy carries beyond the expected date. On the other hand, in a mother who first shows anti-Rh titer *more than 14 weeks* before term, the probability that severe fetal damage will already be present by the time premature induction of labor is feasible is very great. It seems so great that the added risk to the fetus of prematurity and the added hazards to the mother of procedures for premature interruption of pregnancy would make unjustifiable the use of the latter. Those cases in which maternal Rh antibodies appear *between 10 and 14 weeks* before the expected date of confinement would require, in deciding upon premature termination of pregnancy, a nicety of judgment to which, unfortunately, clinical observation and laboratory findings can contribute little further information in the present state of our knowledge.

When the disease is suspected before parturition, for one or another of the reasons we have mentioned, special care should be exercised with



regard to analgesia and anesthesia during labor and delivery. No means should be practiced which reduces the oxygen carried by maternal blood, since the fetus, already struggling to overcome an impaired oxygen-carrying capacity of its blood, will thus be further embarrassed by hypoxemia.

All infants born to Rh-negative mothers should have immediate study of their blood: hemoglobin determination, red blood cell count, count of nucleated red blood cells, Rh determination, and A, B, O blood-group determination. The counts should be repeated at frequent intervals until the possibility of a progressive anemia is ruled out, and careful observation should be maintained for clinical evidence of the disease. In this connection it is important to bear in mind that one of the striking characteristics of hemolytic disease of the newborn is its tendency to manifest itself some days or weeks after delivery. Thus, an infant, apparently normal at birth, may suddenly develop a profound anemia which may go unrecognized if clinical and hematological alertness are relaxed. Moreover, almost all erythroblastotic infants tend to go downhill with increasing speed, and the resulting pathological changes may become irreversible unless treatment is prompt.

Transfusion is the principal method of treatment at the present time. In general, a red blood cell count of three million or less is an indication for it, while a count of two million or less indicates a very poor prognosis and is an urgent indication for transfusion. Routine transfusion, however, of all erythroblastotic babies at birth may subject some of them to unnecessary trauma. Those few cases which present, at the outset, normal newborn hemoglobin levels and red cell counts may suffer more damage from having extra blood crowded into their circulations than from the disease itself. It is advisable in such cases to postpone transfusion until blood studies indicate an actual need for it.

Where Rh incompatibility appears to be the etiology of hemolytic disease of the newborn almost all workers agree that Rh-negative blood should be given. If there is the slightest suspicion of other blood-group incompatibility, Group O blood should be used. Wiener<sup>15</sup> states that when Rh-negative blood other than that of the mother is not available, her blood may be used for transfusion of the infant if the red cells are properly washed free of plasma and resuspended in compatible plasma. It might be safer to use maternal blood in this way only when it is Group O or group-compatible with that of the child.

Erythroblastotic infants should not be permitted to nurse, inasmuch as Rh antibodies are excreted in the mother's milk.

Whereas in the icterus gravis variety of hemolytic disease of the newborn replacement of blood is the principal rationale for transfusion, in the more deadly hydrops fetalis variety the added problem of marked hypoproteinemia is met.

While transfusion combats this to some extent, speculation may be entertained as to whether additional protein, or protein alone in those cases without marked anemia—plasma, for example—might be of value.

Many erythroblastotic infants manifest not only the anemia but also a bleeding tendency. The cause of the latter is unknown, though defective utilization of Vitamin K secondary to liver damage has been called in question. In general these infants do not lack Vitamin K. While its administration probably serves no useful purpose, it certainly can do no harm.

Oxygen therapy, particularly for the icteric and anemic group of infants, has proved to be of some value, especially if the red blood cell count is very low. Whether oxygen therapy to the mother during labor and delivery appreciably aids the fetus remains undecided.

As is evident from the mortality rates, our present treatment of hemolytic disease of the newborn leaves much to be desired. As would be expected from the present state of our knowledge, treatment is actually directed more at symptoms and signs of the disease than it is at causative pathological processes. One gains the impression, for example, that these infants die "liver deaths," that liver damage of various types plays a large part in the clinical picture. Yet at present there are no available treatment methods specifically designed to protect the fetal liver antepartum or to hasten its healing postpartum. Further work along these lines may well reward us with more adequate therapeutic procedures.

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# CALIFORNIA MEDICAL ASSOCIATION

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LEWIS A. ALESEN, M.D.....	Vice-Speaker	DWIGHT L. WILBUR, M.D.....	Editor
JOHN HUNTON.....		Executive Secretary	

FOR COMPLETE ROSTER OF OFFICERS, SEE ADVERTISING PAGE 4

## NOTICES AND REPORTS

### Council Meeting Minutes

*Tentative Draft, Minutes of the 336th Meeting of the Council, California Medical Association*

\* \* \*

The meeting was called to order by Chairman Edwin L. Bruck at 9:30 A.M., September 8, 1946, at the Fairmont Hotel, San Francisco.

#### 1. Roll Call:

Present were John W. Cline, President-elect; E. Vincent Askey, Speaker; L. A. Alesen, Vice-Speaker; Edwin L. Bruck, Council Chairman; L. H. Garland, Secretary, and Councilors Johnston, Crane, Henderson, Anderson, Kneeshaw, Kindall, MacDonald, Green, Cherry, MacLean, Moody, Thompson and Regan.

Present by invitation were C. L. Cooley, Secretary of California Physicians' Service; Dwight H. Murray, Chairman of the Committee on Public Policy and Legislation; Messrs Hartley F. Peart and Howard Hassard, legal counsel; Messrs. Clem Whitaker and Ed Clancy, Public Relations Consultants; Mr. William W. Bowman of C.P.S.; Mr. John Hunton, Executive Secretary; and Messrs. Robert F. Edwards and William P. Wheeler of the C.M.A. office.

A quorum was declared present and acting.

#### 2. Approval of Minutes:

On motion duly made and seconded the minutes of the 198th meeting of the Executive Committee, June 29, 1946, were approved.

On motion duly made and seconded, the minutes of the 331st to 335th, inclusive, meetings of the Council, held May 6 to 10, 1946, were approved.

#### 3. Membership:

(a) A report of membership as of September 6, 1946, was received.

(b) On motion duly made and seconded, 148 members whose 1946 dues had been received since the last Council meeting were reinstated as active members.

(c) On motion duly made and seconded, Doctors Robert O. LeBaron of Mendocino-Lake, William O. Weiskotten of San Diego, William E. Carter of San Francisco, and Earnest Dozier of Shasta County were elected to Retired Membership.

(d) On motion duly made and seconded, Doctors Harry E. Foster of Alameda, Olive B. Cordua and A. M. Lesem of San Diego, Philip A. Bearg of San Luis Obispo and Portia Bell Hume of Alameda County were elected to Associate Membership.

(e) Applications for Retired Membership from two Los Angeles County members who had not maintained active membership since 1943 were discussed and it was decided that the Los Angeles County Medical Association should be notified that the provisions of the Consti-

tution and By-laws must be followed and these applications denied.

#### 4. Financial:

(a) Financial reports showing bank balances as of September 6, balance sheet as of August 31, 1946, and revenues and expenditures for the period ending August 31, 1946, were received.

#### 5. Interim Appointments:

(a) The appointment by Executive Committee Chairman Shipman of Doctor E. L. Bruck and Messrs. Howard Hassard, Clem Whitaker, C. Ray Miller and John Hunton as a committee to select a surveyor to look into the business methods employed by California Physicians' Service was confirmed.

(b) Council Chairman Bruck announced the appointment of a committee composed of Doctors Hamilton Anderson, Nelson Howard, Walter Beckh, T. H. Kelly and Matt N. Hosmer, with John Hunton serving ex-officio, to pass upon advertising offered to CALIFORNIA MEDICINE. These appointments were confirmed.

On the subject of CALIFORNIA MEDICINE, it was moved by Cline, seconded by Alesen and unanimously voted that the Council express to Doctor Dwight L. Wilbur, Editor, its complete approval of the changes effected in the official journal and compliment him on his handling of CALIFORNIA MEDICINE.

(c) On a request from the California State Board of Nurse Examiners for the nomination of four physicians from whom two would be chosen as members of the Advisory Council to succeed Doctors John V. Barrow and Anthony B. Diepenbrock, terms expired, it was voted to authorize the Council Chairman to make such nominations.

(d) The Chairman announced his appointment of Doctor Verne Mason of Los Angeles to succeed Doctor Roy Thomas of Los Angeles, resigned, as a member of the standing Committee on Hospitals, Dispensaries and Clinics.

#### 6. Advisory Planning Committee:

(a) Chairman Hunton reported that the Advisory Planning Committee had held its required meetings. The committee asked and was granted the appointment of two additional members, Joseph Donovan, Executive Secretary of the Santa Clara County Medical Society, and Kenneth Young, Executive Secretary of the San Diego County Medical Society.

(b) The committee called attention to the recently published report of the Assembly Interim Committee on Health Care and proposed that the findings of this committee should be kept alive and made the basis of a positive legislative program by the C.M.A. In this connection

the Advisory Planning Committee offered a three-point program: (1) That the C.M.A. have a positive program of health care legislation; (2) That the Assembly Interim Committee on Health Care report be made the basis of such a program, and (3) That the C.M.A. Executive Committee and Committee on Public Policy and Legislation confer as soon and as frequently as possible with the members of the Assembly Interim Committee on Health Care and with representatives of the State Department of Health in working out such a program.

After discussion it was regularly moved, seconded and voted that these recommendations be approved.

(c) The committee called the attention of the council to the formation of the Bay Area Coordinating Committee by the county medical societies in the San Francisco Bay area. The function of this committee is to implement and expand into neighboring counties the services of the Bureau of Medical Economics established by the Alameda County Medical Association, the function of which is to provide credit, collection and auditing services to the society members and to handle such affairs in a manner to build better public relations and to permit the county society to claim with complete assurance that medical care is available to all county residents at a rate which they can afford to pay. The committee endorsed this movement heartily and expressed such endorsement to the council.

#### 7. Delegate and Alternate to American Medical Association:

Inasmuch as California is now entitled to an additional Delegate and Alternate to the American Medical Association, the Chairman called for nominations for such Delegate and Alternate, to serve until the next meeting of the C.M.A. House of Delegates. On nominations duly made and seconded, Lewis A. Alesen of Los Angeles was elected Delegate and Arthur A. Varden of San Bernardino was elected Alternate.

#### 8. Public Policy and Legislation:

(a) Dwight H. Murray, Chairman of the Committee on Public Policy and Legislation, pointed out that the outlook for health insurance legislation in 1947 was heavily weighted against the profession because of the apparent approval of compulsory health insurance by some highly placed public officials and by large labor organizations. He suggested that the council-approved meetings with members of the Assembly Interim Committee on Health Care and representatives of the State Department of Health be held as soon as possible in order to provide the greatest possible time for working out a positive legislative program for the C.M.A.

Doctor Murray praised the growth of California Physicians' Service to more than 270,000 members but pointed out that even this enrollment out of a state population of close to 10,000,000 was not enough and would have to be augmented.

He suggested that the Council consider sending to England and possibly to France or other European countries a team composed of one physician and one economist. The purpose of such a trip would be to secure up-to-date information on (1) the collection and disbursement of funds under state health insurance systems, (2) the actual percentage of such funds which is eventually spent on direct medical care of beneficiaries, (3) whether or not the people under such systems are actually receiving good medical care, (4) whether or not the people are satisfied with the care they do receive, (5) whether or not the physicians rendering the care are satisfied with the conditions under which they furnish service, and (6) whether or not the type of medical students now being attracted to the medical schools constitute the type of student which would normally be acceptable in this state and country.

(b) Doctors Crane, Regan and Green, recently re-

turned from a meeting of the National Physicians' Committee in St. Louis, reported on the move by that organization to form local committees of physicians for the purpose of interviewing candidates for election and determining the attitude of such candidates toward health insurance proposals.

#### 9. California Physicians' Service:

Doctor Chester L. Cooley, Secretary of C.P.S., reported to the Council the concern of C.P.S. Trustees over the higher expenses incurred by C.P.S. in following out the community enrollment campaigns which are a part of the C.M.A. public relations campaign. Reasons for the higher cost included the need of maintaining more representatives in the field, performing a more extensive enrollment procedure than usual, travel costs, office expenses, telephones, secretarial help and other items. Some modification in the enrollment drives has already been made and is estimated to reduce these higher costs in some degree.

He pointed out that the Trustees of C.P.S. believed that some of these additional costs should not be charged against the normal operating experience of C.P.S. but should be underwritten by the C.M.A. if the community campaigns are to be continued.

Concerning hospitalization, Doctor Cooley told of meetings recently held, looking toward the formation of a joint operating board by Hospital Service of California and Hospital Service of Southern California, under which the two hospitalization organizations would cooperate with C.P.S. and would offer one statewide hospitalization contract. Such a board has already been formed and C.P.S. hopes to effect operating economies under a program of cooperation.

Doctor Cooley also reported that C.P.S. had a membership of more than 270,000 on August 1, 1946, and during August had enrolled 31,000 new members, a new record month.

He requested that the business survey of C.P.S. be authorized and performed at the earliest possible date.

He also stated that there seemed a good chance of securing for San Francisco the central office of Associated Medical Care Plans, Inc., the corporation established by the American Medical Association to correlate the programs of the several state medical care plans and to enlarge existing plans and aid in the creation of new ones.

#### 10. C.M.A. 1947 Annual Session:

The mail vote of the Council of June 4, 1946, on holding the 1947 Annual Session at Hotel Del Coronado was placed before the Council for confirmation. Executive Secretary Hunton reported on the facilities available at Del Coronado and at the major hotels of San Diego, pointing out that it would be necessary to arrange section meetings in two or possibly three places and that Hotel Del Coronado was not able to furnish meals for others than the guests of the hotel itself.

Doctor L. Henry Garland, Chairman of the Committee on Scientific Work, expressed concern over the need of arranging scientific programs in more than one place and stated that available dates for the 1947 session could be secured at the Hotel Biltmore in Los Angeles and the Palace Hotel in San Francisco. After discussion it was regularly moved, seconded and unanimously voted that the mail vote of the council of June 4, 1946, be rescinded and that the 1947 Annual Session be held at the Hotel Biltmore, Los Angeles, on April 30 and May 1 to 3, 1947.

#### 11. Public Relations:

Mr. Clem Whitaker reported that voluntary health insurance campaigns have already been held in 15 counties and are now arranged in San Mateo, San Bernardino and Fresno counties. Editors of 152 newspapers have

been personally contacted in these campaigns and only one editor has declined to cooperate. Mayors of 49 cities have issued voluntary health insurance week proclamations and eleven members of the State Legislature have served as honorary chairmen for such weeks.

He stated that 25 county campaigns will have been completed by July 1, 1947, including Sacramento County in January, 1947, Alameda County in February, San Francisco County in March and Los Angeles County in June.

He stated his firm belief that public opinion toward the medical profession is considerably better today than two years ago. Financially, he reported that the campaign was considerably under the budget voted for 1946 and would finish the year at less than the budgeted figure.

After discussion it was regularly moved, seconded and voted that Mr. Whitaker be authorized to make such time arrangements for the C.M.A. radio program as may be most advantageous.

(b) A resolution of the Monrovia Branch of the Los Angeles County Medical Association, urging the use of additional pamphlets, was referred to Mr. Whitaker for consideration.

## 12. Palo Alto Clinic:

The request of the Santa Clara County Medical Association for a ruling by the Council on the propriety of the contract between the Palo Alto Clinic and Stanford University for the provision of medical services to Stanford students was next discussed. Doctor Russell V. A. Lee, senior partner in the Palo Alto Clinic, appeared, together with Mr. Arnold Rumwell, Clinic Attorney, and Mr. John Stahlaker of Stanford University.

Doctor Lee stated that the contract has now been in effect for five months and is satisfactory to the University, to the students and to the physicians rendering the service. Overhead expenses, he said, amount to only ten cents per month per student, the balance of all funds going to the physicians. He stated that the Clinic and Stanford University both believe that under this contract the students are receiving the best medical service they have ever had.

Referring to a legal opinion furnished by C.M.A. legal counsel and referring particularly to Article VI, Section 3, of the "Principles of Medical Ethics" of the American Medical Association, Doctor Lee discussed the seven features of contract practice which could make such practice unethical. On No. 1, (solicitation of patients) he stated there had been no solicitation by the Palo Alto Clinic. On No. 2 (underbidding to secure contract) he stated there had been no other bid for this service and hence no underbidding. On No. 3 (adequacy of payment to insure good medical service) he stated that good medical care is provided and that the physicians performing the service are satisfied with their compensation. On No. 4 (interference with reasonable competition in the community) he offered to make available to the Stanford students the services of any physician they might select, provided such a procedure would be legal and provided the physicians selected were approved by the medical director of Stanford University. This, he felt, would eliminate any question of interference with reasonable competition. On No. 5 prevention of free choice of physician) he stated that under the present contract the students' choice is limited to the twenty-six physicians comprising the Palo Alto Clinic. He stated that the University interfered to some extent in this situation because some poor results had previously been encountered from free choice and the University felt a responsibility to provide the "best" medical service to its students. He stated his willingness to permit free choice of physicians who were approved by the medical director of the University and to permit the payment of such physicians by the University and the deduction of such payments from the sums due the Palo

Alto Clinic under the contract. On No. 6 (rendering of adequate service to patient) he stated he welcomed an investigation of the service being rendered under this contract. On No. 7 ("contrary to sound public policy") he stated that such determination was vague and stated his belief that sound public policy was being followed.

Doctor Lee stated that Stanford University had four choices open to it in drawing up a student medical care program: It could (1) do nothing and allow the students to shift for themselves. (2) secure a full-time salaried staff of physicians, which it was unwilling to do because it felt the proper quality of men and service could not be secured, (3) contract with California Physicians' Service, which he stated was discussed by the University with C.P.S. but rejected because C.P.S. could not supply the 24-hour service, nursing service, athletic medical care and other features desired by the University, or (4) contract with the Palo Alto Clinic for all services desired.

Doctor Lee offered to answer any questions, either himself or through Mr. Rumwell or Mr. Stahlaker, and various questions were asked and answered.

Doctors Charles Fernish, Fred Borden and John Hunt Shephard, representing the Santa Clara County Medical Society, were then called upon. Doctor Shephard criticized the contract as a step in opposition to the private practice of medicine, pointed out that there is a difference between a student health service and curative medicine and stated that if the panel were opened to permit students to select their own physician, the free choice of physician would still be impaired because of the fact that the medical director of Stanford University is also a partner in the Palo Alto Clinic and could not be considered an unbiased judge because of that affiliation.

Doctor Burt L. Davis, Jr., of Palo Alto stated his belief that the University should permit the students a free choice of physician and should maintain records of payments to physicians on a unit basis, paying both clinic members and others on an equal basis, figured periodically.

Doctor H. T. Browne of Palo Alto stated his belief that medical opinion would not approve of the University medical director also serving as a member of the Palo Alto Clinic.

At this point the council went into executive session.

## 13. Legal Department:

(a) Mr. Hassard reported that the Industrial Accident Commission had agreed to permit the insurance carriers to appear before it on September 17 to discuss the adoption of the fee schedule approved by the Commission on June 18, 1946. The C.M.A. will also appear at that time.

(b) Doctor MacDonald reported on conference with the California Unemployment Stabilization Commission relative to the adoption of sound medical procedures and simplified report forms to be used in connection with the Sickness Disability Law adopted by the 1945 session of the Legislature. He requested approval of a schedule of fees for examination of doubtful cases and suggested that the appropriate fees in the C.M.A.-sponsored industrial fee schedule be used. This calls for \$7.50 for a routine examination, \$15 for a more thorough examination by a specialist and \$25 to \$50 for a complete examination, together with a review of the record, by a specialist. On motion duly made and seconded, it was voted that such a fee schedule should be approved for transmittal to the Unemployment Stabilization Commission, with the understanding that charges for laboratory services or other special diagnostic procedures would not be included in such fees.

Doctor MacDonald also asked for suggestions for a medical director for this work at a salary of \$7,500 annually. Several names were suggested, these to be sent by the C.M.A. to Doctor MacDonald for delivery to the State.



#### 14. California Physicians' Service: (Second appearance)

Mr. Bowman called attention to the request made earlier by Doctor C. L. Cooley that the C.M.A. underwrite the additional expenses to C.P.S. in the community campaigns particularly since such expenses are not ordinary business expenses and should be considered as public relations expenses of the C.M.A. On motion by Kneeshaw, seconded by Kindall and amended by Cline with the approval of the mover and seconder, it was voted that C.P.S. be reimbursed by the C.M.A. for approximately

\$5,700 of such additional expense already incurred and that similar expenses be met by the C.M.A. until further consideration is given this matter at the next Council meeting.

#### 15. Time and Place of Next Meeting:

It was agreed to hold the next council meeting at the time and place selected by the chairman, with the understanding that the fall meeting is by custom held in Los Angeles.

#### 16. Adjournment.

### **California Physicians' Service — Public Relations**

"Make the California Physicians' Service as simple and efficient as possible—and let the public know it."

With the statement as a criterion, the California Physicians' Service one year ago established a new department within the organization: the Department of Public and Professional Relations.

The need was imminent. C.P.S. since 1939 had grown into a California landmark of free enterprise. A nationally recognized plan for the prepayment of medical service, its tremendously accelerated growth called for departmental liaison between the medical profession and beneficiary members. Specifically required was the proper dissemination of technical and general information to the physicians, members and the public. Additionally, the Department's activities were slated to set up an always available question and answer bureau for claim filers. Most important, the Department would be charged with preserving a favorable attitude toward the California Physicians' Service by the physicians and the public.

Today, the Department of Public and Professional Relations, with central offices in San Francisco and Los Angeles, can point with a measure of pride to some of the past year's accomplishments.

Reflecting the considered and growing need for expansion within the department, two more offices (San Jose and San Diego) have added full time public and professional relations personnel to their staffs. This is another step toward providing on-the-spot answers to the problems and questions of physicians and nurses.

In any program developing as rapidly as C.P.S., where the unpredictable human element is such an important factor, questions and misunderstandings are bound to arise. Unless prompt action and counsel is available, the problem can grow into proportions which eventually will lead to an irreparable rift. To iron out such difficulties, professional relations men provide the "in-between" touch.

Relatively, the California Physicians' Service is new—and controversial. Staff personnel are emphasizing that here is a high type of medical care program operating successfully and with the backing of more than 7,400 family doctors. At the same time, no small part of their efforts is directed toward arousing public antipathy over the social and public dangers of compulsory health insurance.

Advocates of state medicine are increasing their efforts statewide and nationally. The 1947 meeting of the State Legislature may see a renewal of the bitter fight for compulsory health insurance. The Truman-approved Wagner-Murray-Dingell Bill has been approved by the Senate Education and Labor Subcommittee on Health and Education.

Finding that voluntary health insurance plans were inadequate to meet "all of the requirements of the nation," the subcommittee's report concluded:

"To cover everyone, the adverse as well as the good risks, the young and the old, the sick and the well, the rural and the city dwellers, the low and the high income

groups, the poor and the rich areas, all this takes a mechanism as representative and all-inclusive as a national health program, built around a system of prepaid medical care."

The report concluded that such a system must be financed by "required contributions to the social-security fund and by payments from general tax revenues."

The Public and Professional Relations staff is in the forefront of the battle against this evident attempt at regimentation of the medical profession. In every service club, fraternal organizations and in rural schoolhouses, staff speakers are hammering at the theme: "The California Physicians' Service, or any form of voluntary health insurance, can give the public a more economical and broader plan of coverage than could any politician under any system of government controlled medicine!"

Perhaps to the title, "public and professional," could be added "political." While promoting better physician-patient relations within the organization, staff personnel know and emphasize that this is also a political battle.

In January of this year, the Department of Public and Professional Relations joined forces with the Whitaker-Baxter organization, public relations counsel for the California Medical Association, in coordinating an impressive radio and advertising campaign. Under the direction of the Whitaker-Baxter staff, public speeches, radio and newspaper publicity, pictures, and advertisements are acquainting the California public as never before with the worthwhileness of C.P.S. benefits in particular and voluntary health insurance in general.

C.P.S. physician-members especially are rallying to the defense of good medicine and are proving to the public that they can bring their system of medical economics into pace with the rapid advance of their medical science.

Increased enthusiasm throughout the entire Service was evidenced recently when the State Supreme Court ruled that C.P.S. was not subject to regulation by the Insurance Commissioner. Particularly applicable, from the professional relations standpoint, was the Court's conclusion: "Probably there is no more impelling need than that of adequate medical care on a voluntary low cost basis. The medical profession, unitedly, is endeavoring to meet that need. Unquestionably, this is a service of a high order and not indemnity."

Telling California's 9,000,000 citizens about this "service of a high order" is part of the responsibility of the Department of Public and Professional Relations. The department is looking forward to the day when district offices will each have a representative on the spot to provide immediate service to physicians, members, and the public.

When the present quarter million membership has passed the million mark, this department may take pride in declaring:

"The California Physicians' Service is as simple and efficient as possible—and the public knows it!"

[Roster of C.P.S. officials is printed on advertising page 3.]



# NEWS and NOTES

## NATIONAL • STATE • COUNTY

### ALAMEDA

**Permanente Foundation**, which operates a pre-paid medical care service, has bought the 123-room Piedmont Hotel in Oakland, not far from the old Fabiola Hospital which was taken over by the Foundation several years ago. The hotel property, purchase price of which is reported at about \$200,000, will be used as a nurses' home and training center. Although Permanente Foundation was set up originally by Mr. and Mrs. Henry J. Kaiser to provide medical care for workers in Kaiser enterprises, it is reported that at present some 85 per cent of patients are not Kaiser employees.

### DEL NORTE

The California Medical Association is ready to assist Del Norte County financially in setting up a cancer detection clinic at Crescent City. Mrs. Ralph Luick reported to the county board of supervisors upon her return from the annual meeting of the California Cancer Society in San Francisco. Mrs. Luick, commander of the county Cancer Society, reported also on the substantial program organized by the national and state Cancer Society units for the necessary early detection of cancer.

### GLENN

Plans for a health unit to be financed by Glenn and Colusa counties have been rejected by the Glenn County board of supervisors. A spokesman for the supervisors said that the board was looking toward construction of a new county hospital and was reluctant therefore to spend money on the proposed bi-county health unit.

### LOS ANGELES

Dr. Arthur J. Moss is now associated with Dr. Lawrence M. Hill in the practice of pediatrics in Inglewood. Dr. Moss, a graduate of the University of Minnesota, spent 22 months in Australia, New Guinea, Luzon and Japan with the U. S. Army Medical Corps.

Dr. Homer Rosenberger, Jr., has returned to Whittier to the practice of medicine after serving four years as Chief of Medical Service in the U. S. Army Air Corps Station hospitals. Dr. Rosenberger, a graduate of Stanford University Medical School, is the son of the late Dr. H. G. Rosenberger, prominent Whittier surgeon for 30 years.

Dr. Russell W. Starr, Los Angeles physician, was elected commander of the Fourth Area, Department of California, American Legion, at its convention in San Francisco. The Fourth Area comprises seven Legion districts—in Santa Barbara, San Luis Obispo, Ventura and Los Angeles counties. Dr. Starr has been a member of the Legion since its inception and has represented it on many civic committees in Los Angeles.

Dr. Nathan Jacobs now occupies the new medical building at 80 West Sierra Madre Blvd., Sierra Madre. Dr. Jacobs, who spent two and a half years in military service, had previously practiced in Sierra Madre.

Dr. Mary B. Dale, 1035 East Howard Street, a member of the Los Angeles county health department medical staff, has been appointed epidemiologist for the department according to Dr. Roy O. Gilbert,

acting county health officer. Dr. Dale is the first woman to hold such a position in Los Angeles County.

Dr. S. H. Welch, whose offices were in the Security Building, Glendale, retired from practice on August 1. The eye, ear, nose and throat specialist had been in practice 41 years.

Dr. Russell O. Spittler has become associated with Dr. W. J. Tension in the practice of general surgery with offices at 38 E. Huntington drive. Dr. Spittler, who was recently discharged from the medical corps of the U. S. Army, is also on the staff of St. Luke's Hospital in Pasadena. He is a graduate of Minnesota Medical School.

Dr. Mark Giffords, recently discharged from the U. S. Army Medical Corps, has opened offices at 8730 El Manor Ave., Westchester. Dr. Giffords graduated from Boston University School of Medicine in 1935 and served internships at Madison, Wisconsin, and Perth Amboy, New Jersey.

Dr. Harold M. Walton has been appointed medical superintendent of White Memorial Hospital. He succeeds Dr. Orlyn B. Pratt, who has been called to head the department of pathology for the College of Medical Evangelists, Loma Linda and Los Angeles.

Dr. Howard F. West was elected president of the American Heart Association to succeed Dr. Roy W. Scott of Cleveland, the Association announced. Dr. West was one of the founders of the Los Angeles Heart Association and the California Heart Association. He has served as president of both groups. A graduate of Stanford University School of Medicine, he now serves as clinical professor of medicine in the University of Southern California School of Medicine. He is president of the Los Angeles Academy of Medicine, chairman of the Medical Advisory Committee of General Hospital, member of the board of directors of both the Los Angeles County Tuberculosis and Health Association and Combined Christmas Seal Fund and a member of the Health Service Committee of the Welfare Council of Metropolitan Los Angeles.

Courses in public health and public health nursing will be included in the new fall schedule of evening courses which University of California Extension will open in downtown Los Angeles in late February according to Miss Margaret Wotton, Class Organizer.

Dr. K. H. Sutherland, District Health Officer for the Los Angeles County Health Department will conduct a course in Public Health and Preventive Medicine, scheduled to open Wednesday evening, September 25 at 7 o'clock for 18 weekly meetings.

### ORANGE

Dr. Joseph A. D'Alessio has established his medical and surgical offices in more spacious quarters, at the Palm Springs Medical-Dental Centre, 244 South Palm Canyon Drive. Dr. D'Alessio has been in private practice in Palm Springs since his discharge from the United States Army Medical Corps.

### SACRAMENTO

Hilding R. Johnson, M.D., has announced the opening of his new offices at 2100 Capitol Avenue, Sacramento.

## SAN DIEGO

Dr. S. J. McClendon, San Diego pediatrician and president of the California Medical Association, at the invitation of the **Brazilian government**, read a paper on rheumatic fever at the first **Inter-American Medical Congress** at Rio de Janeiro early in September. The congress is sponsored by the Academy of Medicine at Rio de Janeiro in cooperation with the Brazilian and United States governments and the U. S. Public Health Service.

## SAN FRANCISCO

Dr. William J. Kerr, professor of medicine, and Dr. John J. Sampson, associate clinical professor of medicine of the **University of California Medical School**, will deliver papers to the **Second Inter-American Congress of Cardiology** in **Mexico City**, meeting from October 6 to 12. Dr. Theodore Althausen, associate professor of medicine at the same school, recently returned from Mexico City where he delivered a scientific paper before the **First Mexican Medical Congress**.

Plans for the **Maimonides Health Center** for the chronic sick, on which construction is expected to start next year, will be drawn by Eric Mendelsohn, architect, it is announced by Joseph M. Bransten, chairman of the building committee.

The health center, which is to cost an estimated \$575,000, will be located on **Sutter Street** near **Mount Zion Hospital** so that the hospital's facilities may be used. It is said to be the first center for care of the chronic sick of the Pacific Coast.

## SAN LUIS OBISPO

Dr. H. O. Swartout, internist, has announced the opening of a medical office at 412 North Broadway, **Santa Maria**. Formerly on the staff of **White Memorial Hospital**, Dr. Swartout was also Health Officer for Los Angeles County.

## SAN MATEO

Twenty-six rooms in **San Mateo County's Community Hospital** which could be used for patients cannot be opened because of a **shortage of nurses**, according to Dr. Harold Raycroft, recently appointed hospital director. He said that 14 more nurses would be needed if the rooms are to be put into use.

The director said that although the hospital with its present staff does not have to turn away patients who need medical attention, if the additional nurses were available some patients could be kept longer and it would not be necessary to draw such fine distinctions as to who does and who does not need hospitalization.

Requirement that the county health director be a California licensed physician is one of a number of San Mateo County charter changes which are proposed for submission to voters in the general election next November.

## SANTA BARBARA

Centralization of the facilities of **Santa Barbara County General Hospital** was recommended by Dr. Philip K. Gilman in a report following a survey which he made as chief of the Bureau of Hospital Surveys of the California State Department of Health. Recommendations included one to construct a multi-story main building to house facilities now scattered in small units over the extensive grounds, which are several miles outside the city limits of Santa Barbara. Possibility that the County Health Department might be quartered at the hospital rather than in the court house also was suggested by Dr. Gilman.

## SONOMA

Dr. William J. Rudee, recently discharged from the Navy, has opened temporary offices at 1055 Fourth street, **Santa Rosa**, where he will resume his practice until more centrally located office space is available. Before entering the service, Dr. Rudee was a practicing physician and surgeon in Santa Rosa.

Dr. J. A. Fowlie has sold his office in **Cotati** and announced that hereafter he will devote all his time to his Santa Rosa office.

Dr. Marian B. McAulay has opened a new office at 226 Washington Street, in **Petaluma**.

## YOLO

Dr. W. J. Blevins, Jr., has announced the proposed construction of a \$30,000 Physicians' building in **Woodland**. Construction probably will start late this year or early in 1947, Dr. Blevins said. The structure will house Dr. Blevins' offices and those of Dr. John O'Hara, who now practices in the Porter Building.

Dr. W. J. Blevins, Sr., recently retired from practice after suffering a heart attack. His condition now is reported greatly improved.

## GENERAL NEWS

**Surplus medical equipment**, for purchase of which veterans of World War II can obtain priority, is listed in a catalog put out by the War Assets Administration. Catalogs and information as to how to apply for purchases are available through two regional offices of the WAA in California. In **Los Angeles** the address is: George F. Ballif, Jr., Regional Director, War Assets Administration, Mode o' Day Building, Hill Street and Washington Boulevard. Los Angeles office telephone number is Richmond 2311. The **San Francisco** address is Leland D. Dedo, Regional Director, War Assets Administration, 30 Van Ness Avenue, and the telephone number is Underhill 2425.

California has been allotted \$185,820 for hospital survey and planning and \$1,957,875 for construction under the five-year hospital construction program authorized in the federal Hospital Survey and Construction Act, according to figures released by Surgeon General Thomas Parran of the United States Public Health Service. The act authorizes appropriation of \$3,000,000 for surveys and \$75,000,000 annually for five years for hospital construction in the United States.

Three evening courses in graduate medicine are being offered this fall by the University of Southern California School of Medicine. A course in **Quantitative Methods in Medicine**, beginning October 2, will be conducted by Frederick Moore, M.D., and associate. Lectures each Wednesday evening for 12 weeks will cover the collection, analysis, interpretation and presentation of medical data. Travis Winsor, M.D., will conduct a course in the **Clinical Aspects of Electrocardiography**. The course begins November 5, and meetings will be each Tuesday evening for 12 weeks. A course in **Cardiovascular Diseases**, under the direction of George C. Griffith, M.D., and associates, began September 16. Meetings are Monday evenings for 12 weeks.

Inquiries should be addressed to Director, Division of Graduate Medicine, School of Medicine, University of Southern California, Room 2721, Los Angeles County Hospital, Los Angeles 33, Calif.

Dr. John Parkinson, National Heart Hospital, London, and Dr. Helen B. Taussig, Johns Hopkins Hos-

pital, Baltimore, will be the guest speakers at the annual symposia of the **California Heart Association** to be held in San Francisco, Los Angeles and San Diego, October 16 through 25.

Dr. Parkinson is consulting cardiologist to the Royal Air Force and was chief assistant to Sir James Mackenzie before World War I. He is in charge of the Cardiac Department of the London Hospital and of the National Heart Hospital. Among Dr. Parkinson's topics will be recent developments in cardiac radiology and a discussion of rheumatic fever.

Dr. Taussig and her associate, **Dr. Alfred Blalock**, are noted for their successful treatment of congenital heart disease. Dr. Taussig will report on the conception and development of the surgical treatment of congenital heart disease.

**Physicians may register** for the symposia at the following addresses: San Francisco, October 16-19, San Francisco Heart Committee, 604 Mission Street, San Francisco 5, California. Los Angeles, October 23-25, Los Angeles Heart Association, 117 West 9th Street, Los Angeles 15, California. Registration for the San Diego meeting, October 21, can be made through the San Diego County Medical Society.

**The American Legion** of California, at its August convention in San Francisco, **reaffirmed its 1945 opposition to compulsory health insurance** legislation with a warning against increased tax burdens and regimentation of the medical profession.

Recalling that its Rehabilitation Commission, responsible for the rights and welfare of disabled wounded service men, had protested last year against proposed plans for compulsory health insurance, the Legion's resolution declared that California's more than 1,000,000 veterans who have served in the armed forces now have available to them hospital and medical care provided by the United States Government. Pay roll deductions that may be forced on the veteran to pay for compulsory health insurance would be **"a cost for services already supplied."**

Calling attention to the "countless voluntary health insurance plans now being offered by the physicians and the insurance companies," the Legion's resolution, brought to the floor by national executive committeeman Leon Happell, Stockton, declared:

"Proposed plans of compulsory health insurance would increase the tax burden and bring about regimentation of the medical profession."

The Legion resolution concluded with the statement that **all forms of compulsion are incompatible with our American way of life** "since our liberties and opportunities would be circumscribed."

The 5,000 convention delegates represented approximately 170,000 California Legionnaires.

**Publication of a new journal**, the Quarterly Review of Dermatology and Syphilology, has been announced by the Washington Institute of Medicine, Washington, D. C. The new publication will survey all published material on Dermatology and Syphilology appearing anywhere in the world from January 1, 1946, onward. **Donald M. Pillsbury, M.D.**, is editor-in-chief, with **Herman Beerman, M.D.**, and **Clarence S. Livingston, M.D.**, as associate editors. The editorial board includes specialists from universities and medical centers throughout the world. The complete board will be announced by Dr. Pillsbury in the near future.

## In Memoriam

**Austin, Lloyd Crockett.** Died at Los Angeles, July 3, 1946, age 53. Graduate of the St. Louis University School of Medicine, Missouri, 1928. Licensed in California in 1928. Doctor Austin was a member of the Los Angeles County Medical Association, the California Medical Association, and a Fellow of the American Medical Association.

**Beck, Homer Henry.** Died at Corning, July 21, 1946, age 61. Graduate of the Jefferson Medical College of Philadelphia, Pennsylvania, 1910. Licensed in California in 1919. Doctor Beck was a member of the Tehama County Medical Society, the California Medical Association, and the American Medical Association.

**Davies, Benjamin Paul.** Died at Palo Alto, July 8, 1946, age 41. Graduate of the University of Kansas School of Medicine, Lawrence-Kansas City, 1931. Licensed in California in 1938. Doctor Davies was a member of the Santa Clara County Medical Society, the California Medical Association, and the American Medical Association.

**Jacobs, Louis Olive.** Died at San Francisco, April 29, 1946, age 66. Graduate of the University of California Medical School, Berkeley-San Francisco, 1904. Licensed in California in 1904. Doctor Jacobs was a member of the San Francisco County Medical Society, the California Medical Association, and a Fellow of the American Medical Association.

**Kemper, Christian Arthur Schultz.** Died at Escondido, July 13, 1946, age 63. Graduate of the Medico-Chirurgical College of Philadelphia, 1908. Licensed in California in 1920. Doctor Kemper was a member of the San Diego County Medical Society, the California Medical Association, and the American Medical Association.

**Libby, Arthur A.** Died at Pasadena, July 23, 1946, age 81. Graduate of the University of Southern California School of Medicine, Los Angeles, 1897. Licensed in California in 1897. Doctor Libby was a Retired Member of the Los Angeles County Medical Association, the California Medical Association, and an Affiliate Fellow of the American Medical Association.

**McDaniel, John Lavender.** Died at San Fernando, July 20, 1946, age 63. Graduate of the University of Georgia School of Medicine, Augusta, 1883. Licensed in California in 1909. Doctor McDaniel was a Retired Member of the Los Angeles County Medical Association, and of the California Medical Association.

**Silvia, Clara Agnes.** Died at Gilroy March 13, 1946, age 69. Graduate of the College of Physicians and Surgeons, San Francisco, 1903. Licensed in California in 1903. Doctor Silvia was a member of the Santa Clara County Medical Society, the California Medical Association, and the American Medical Association.

# INFORMATION

## COURT HOLDS C.P.S. NOT SUBJECT TO INSURANCE LAWS

California Physicians' Service is a service corporation, it is not subject to restrictive laws governing insurance companies and its operations are not under supervision of the California Insurance Commissioner. This is the import of a decision by the California Supreme Court, announced late in August, successfully climaxing for C.P.S. an action at law which that organization had begun in San Francisco Superior Court in 1940.

When C.P.S. was formed in 1939 as a service corporation, the insurance commissioner objected and contended that it was in reality an insurance company and subject to all of the restrictive laws governing insurance. Counsel for C.P.S., Hartley F. Peart and Howard Hassard, advised both the California Medical Association and C.P.S. that in their opinion the rendering of medical care on a prepaid basis through a service corporation in which all doctors of medicine were free to participate, was a professional matter and not an insurance business.

Accordingly, C.P.S. commenced an action against the insurance commissioner for a declaratory judgment. The suit was commenced in 1940. In it C.P.S. sought a judgment of the court establishing its legal right to engage in a prepaid medical service plan. The case was heard by Judge C. J. Goodell, then of the Superior Court in San Francisco, and was decided in favor of C.P.S. The insurance commissioner appealed. The case finally reached the California Supreme Court, and on August 27, 1946, the Supreme Court in an opinion written by Justice Douglas Edmonds decided in favor of C.P.S. and against the insurance commissioner. Six of the seven justices of the California Supreme Court concurred in the main opinion, and one justice concurred in a separate opinion.

As the decision of the Supreme Court is one of first impression, it is a milestone upon the path of voluntary prepaid medical care. Its major features, with certain portions of the opinion and footnotes summarized, follow:

California Physicians' Service, a non-profit corporation (Civ. Code sec. 93-605e), sued to obtain a declaratory judgment that it is not engaged in the business of insurance within the meaning of the regulatory statutes of this state. The insurance commissioner has appealed from a determination adverse to his contentions, and the principal question for decision concerns the organization's right to operate, without his supervision, for the purpose of defraying the expense of medical care incurred by its dues-paying members.

The stipulation by which the evidence in the case was presented to the trial court shows the following facts:

The corporation was organized by the medical profession in 1939 to meet the need of persons in the lower income groups for medical care and surgical service. It holds a certificate of compliance with the provisions of section 593a of the Civil Code, relating to health service corporations, issued by the State Board of Medical Examiners. The incorporators were all officers and councilors of the California Medical Association, an association comprising over 5,000 doctors of medicine practicing in the State of California and constituting a component state unit of the American Medical Association. The Service is a pioneer attempt by the physicians and surgeons of California to make available medical care for those who desire it and, because of financial limitations find the cost of sickness a burden not easy to bear.

The articles of incorporation state that the organization was formed "after more than ten years of continuous investigation and study." As a summary of policies and purposes, it is said "that the duties and obligations of the profession are not only leadership in the maintenance of high standards of medical service but also in the means of distribution of that service so that all who need it may receive it; that the very advances made by modern science have greatly increased the cost of good medical service and hospital care and will continue to increase that cost as new methods and equipment for diagnosis and treatment are discovered and perfected . . . that a method which only the medical profession can most effectively provide is necessary properly to distribute this cost of medical service so as to relieve the intolerable financial burden heretofore falling on the unfortunate few in any given period of time; that the establishment by the profession of a voluntary medical service plan, participated in by all doctors of medicine desiring to do so, will enable the people of the State of California to obtain prompt and adequate medical attention and hospital care whenever needed on a periodic budgeting basis without injury to the standards of medical service, without disruption of the proper physician-patient relation and without profit to any agency, and will assure that all payments made by patients, except administrative costs, will be utilized for medical service and hospital care and not otherwise; that such a plan will create an efficient public and civic service without commercial exploitation of the patients or the profession or any restriction of an individual's fundamental right freely to select, when his need arises, the doctor of medicine and hospital desired by him; and finally, such a coordinated organized service can, upon the same fundamental basis, be the means which governmental agencies—federal, state, and local—may use to provide, at the lowest possible cost to the taxpayer, good medical service and hospital care for the indigent, needy or handicapped residents of California. . ."

To make effective these broad objectives, the by-laws declare that every resident doctor of medicine who holds "a valid and unrevoked physician's and surgeon's certificate issued to him by the Board of Medical Examiners of the State of California shall be invited by the board of trustees to become a professional member . . . it being one of the fundamental purposes of this corporation that professional membership . . . shall embrace all legally licensed Doctors of Medicine . . ." The professional members select, on a basis of state-wide representation, the administrative members, limited to 75, each of whom must be an active member in good standing of the California Medical Association. The voting rights in the corporation are vested in the administrative members exclusively. They elect the directors who are designated as trustees.

The persons who are to receive medical attention from the professional members "on a periodic budgeting basis" are termed beneficiary members . . . (the court describes in detail the contracts with beneficiary members) . . .

The Rural Health Service Agreement which the corporation made with the Farm Security Administration, an agency of the United States, contains substantially the same terms as those of the Group Medical Service Agreement, but there are additional provisions for hos-



pitalization and reimbursement for drugs. Although it is stated in the preamble of this agreement that it is of an experimental nature and binding only for a specified period, the stipulation of facts recites that it "has been adopted by California Physicians' Service and is in use at the present time."

... (Rural Health Service Agreement is summarized) ... Each professional member agrees, by written contract with the corporation, to render such needed medical attention to beneficiary members as may properly be requested of him and, for the payment of compensation for such services, to look solely to the available funds of the organization. But every physician "is free to exercise his individual right to refuse to accept any person as a patient." The amount to be paid to a physician is determined by what is known as a unit system, and each professional member agrees to accept as payment in full for his services rendered to beneficiary members during each month a pro rata distribution of that portion of dues collected during such month.

The by-laws describe the unit system and its operation as follows: "By the term 'unit system' is meant a method of computing the compensation due to professional members rendering medical or surgical services whereby a proportional valuation is set upon each kind of service by counting each such service as a determined number of units by resolution of the board of trustees adopting a schedule or schedules of compensation. The total sum of money available for compensation of professional members is divided by the total number of units of service rendered during any given period to determine the monetary value of a single unit for the purpose of compensation earned by professional members and each professional member is paid according to the number of units of service he has rendered in said period. ...

"In the event that during any period there is available for payment to professional members a sum in excess of the sum necessary to pay the full schedule or compensation established by the board of trustees such excess sum shall be reserved by the board of trustees as a part of the reserve funds of the corporation or if the board of trustees so determines, it may be distributed on a unit system to those professional members who have in any prior period determined by the board received for their services less than the compensation schedule, provided no professional member shall thereby receive more than the full compensation schedule for any service rendered."

Upon this evidence the trial court decreed as follows:

"That rendition of medical and surgical services by the professional members of ... California Physicians' Service, and the acceptance of payment for such services ... from funds contributed by the beneficiary members" of the organization "does not constitute the transaction of an insurance business under the insurance laws" of this state. More generally the court declared that the "objects and purposes set forth in the articles of incorporation" of the Service "are lawful objects and purposes and the performance or undertaking by plaintiff of any or all of said objects does not and will not violate any ... laws of the State of California relating to the business of insurance." Concerning the medical attention which the members receive, the decree recites that "the rendition of medical and/or surgical services ... does not constitute a violation of the principle that a corporation may not engage in or be licensed to practice one of the learned professions ... ." But the court declared that the collection of money "to be used in the manner and for the purposes outlined in the articles of incorporation of the plaintiff" subjects it to regulation by the Attorney General of California in accordance with the provisions of section 605(c) of the Civil Code relating to non-profit corporations.

As grounds for reversal of the judgment, the insurance commissioner declares that the courts should not place judicial approval upon a controversial type of new business enterprise; also that in the absence of specific statutory authority for declaratory relief against the state or an officer of the state such an action cannot be maintained. The term "person" as used in section 1060 of the Code of Civil Procedure, it is urged, does not include the state or its officers because general words in a statute which might have the effect of restricting governmental powers are to be construed as not applying to the state, and declaratory relief is not available against political subdivisions of the state.

Another contention of the commissioner is that the Service's activities constitute the unlawful practice of medicine by a corporation. Furthermore, he says, section 593a of the Civil Code specifying certain minimum requirements which a health service corporation must meet, and a statute authorizing political subdivisions of the state and public agencies to contract with a non-profit membership corporation for medical service (Stats. 1939, Ch. 250; Deering Gen. Laws 1943, Act 3725) are invalid. These enactments, it is claimed, make an unreasonable classification because the grant of the privilege of corporate practice, based upon the number of licensee members of the corporation, is not related to qualification or fitness. Also, the argument continues, no subsequent legislation has authorized the activities of the Service.

The major ground for the attack upon the judgment is that the Service is engaged in the business of transacting insurance and therefore is subject to the regulatory laws governing such corporations. All of the elements of insurance are present in the Service's plan, says the commissioner. There is no real distinction between service and insurance, and by its contracts the corporation has obligated itself to furnish medical care. The Service's plan of operation is not excepted by statute from the supervision of the insurance department, and the Service is not a consumer cooperative, but a corporation organized for the profit of the professional members. The nature of the medical service, and of the contracts it offers, require the application of the insurance laws to its affairs in order to prevent exploitation of the public. Finally, the commissioner asserts, the judgment goes beyond the stipulated facts in prospectively validating future acts not comprehended in the Service's plan of operations as conducted at the time the decree was entered, and its method of doing business since the notice of appeal was filed shows the necessity for state insurance regulation.

In response to the contentions of the attorney general the Service asserts that declaratory relief is a proper form of action against the insurance commissioner. Also, it replies, the Service is not engaged in the corporate practice of medicine; if so, its functions are expressly permitted by statute.

Turning to the most important question, the Service declares that it is not engaged in the insurance business but is rendering personal service, as distinguished from indemnity, compensation for which is limited to the resources of a pooled fund; that the professional members, not the Service, assume any and all risk; and that it is actually a producer-consumer cooperative. Furthermore, the Service concludes, as a matter of social policy the state, by statute, has declared that a non-profit membership corporation may lawfully defray or assume the cost of medical and surgical services or render any such service. In that regard the argument runs, the legislature has necessarily determined that the rendition of medical and surgical services by a non-profit membership corporation coming within the purview of section 593a of the Civil Code does not constitute that type of insurance assuming it is insurance which is subject to regulation by the

insurance commissioner. In conclusion, the Service maintains that the legislative classification under the applicable code provisions is constitutional.

... (the Court reviews prior cases and decides that a declaratory judgment action is proper) ...

Considering the merits of the case, it is a matter of common knowledge that there is great social need for adequate medical benefits at a cost which the average wage earner can afford to pay. Unquestionably the distribution of these services has lagged far behind production. During the past several decades many plans have been devised to distribute the cost of medical care (see: *People v. Pacific Health Corp.*, 12 Cal. 2d 156; *Butterworth v. Boyd*, 12 Cal. 2d 140; *Pacific Employers Ins. Co. v. Carpenter*, 10 Cal. App. 2d 592; 52 Harv. L. Rev. 809-817) and in 1917, the California legislature adopted a constitutional amendment calling for the creation of a system of state medicine financed through taxation (Stats. 1917, p. 1948). This amendment was rejected by the people.

In 1935, similar legislation met defeat. The medical profession then undertook the responsibility for providing medical service on an ability-to-pay-for basis, and it is obvious that the legislature, by enacting section 593a of the Civil Code,<sup>1</sup> expressly authorized the organization of corporations such as California Physicians' Service. By this enactment, the state's social policy in regard to the corporate practice of medicine, to the limited extent specified, has been determined and the courts are bound thereby. (See: *People v. Pacific Health Corp.*, *supra*, p. 161; *Pacific Employers Ins. Co. v. Carpenter*, *supra*, p. 602; 52 Harv. L. Rev. 809-817; 25 Cal. L. Rev. 91-98; 53 Yale L. J. 162-182.) It is stipulated that the Service has complied with the provisions of this statute and holds a certificate in the form authorized by its provisions.

The statutory provisions authorizing the Service's operations do not violate Art. IV, sec. 25, subd. 19, of the California Constitution which prohibits "granting to any corporation, association, or individual any special or exclusive right, privilege, or immunity." As stated in *Livingston v. Robinson*, 10 Cal. 2d 730, 740: "The question of classification is generally one for the legislative power, to be determined by it in the light of its knowledge of all the circumstances and requirements, and its discretion will not be overthrown unless it is palpably arbitrary. (*Wores v. Imperial Irr. Dist.*, 193 Cal. 609.) It will be presumed that the legislature made inquiry to determine whether or not there were evils to be remedied and that the classification made was based upon the result of the

inquiry." And in *People v. Western Fruit Growers*, 22 Cal. 2d 494, 507, it was said: "When a legislative classification is questioned, if any state of facts reasonably can be conceived that would sustain it, there is a presumption of existence of that state of facts, and the burden of showing arbitrary action rests upon the one who assails the classification." (See also: *Gillum v. Johnson*, 7 Cal. 2d 744, 759; *State Bar v. Superior Court*, 207 Cal. 323, 332; *People v. Keith Ry. Equip. Co.*, 70 A.C.A. 445, 461.) The legislature may classify organizations rendering medical services under the same general principles as those which allow it to license for numerous occupations and professions and public policy certainly permits restriction of the right to assume the cost of such services to such organizations as meet reasonable and definite standards. The interest of the state in the health of its citizens (see: *Butterworth v. Boyd*, *supra*) fully justifies the legislative classification. The decision relied upon by the attorney general, *Van Camp Sea Food Co., Inc. v. Newbert*, 76 Cal. App. 445, to support his conclusion is in accord with these general principles but is factually distinguishable.

Considering the question as to the supervision which the state has imposed upon corporations such as the Service, the legislature has defined insurance as "a contract whereby one undertakes to indemnify another against loss, damage, or liability arising from a contingent or unknown event." (Insurance Code, sec. 22; Civil Code, sec. 2527.) Disability insurance "includes insurance appertaining to injury, disablement or death resulting to the insured from accidents, and appertaining to disablements resulting to the insured from sickness." (Insurance Code, sec. 106.) Under Chapter 4 (sec. 10272) of the Insurance Code, which deals with standard provisions in disability policies, "indemnity" is said to mean "benefits promised"; while in the Civil Code, sec. 2772, it is defined as "a contract by which one engages to save another from a legal consequence of the conduct of one of the parties, or of some other person." Otherwise stated, "insurance generally may be defined as an agreement by which one person for a consideration promises to pay money or its equivalent, or to perform some act of value, to another on the destruction, death, loss or injury of someone or something by specified perils." (29 Am. Jur., p. 47.)

These definitions clearly state the basic concepts or elements which are a necessary prerequisite of a contract of insurance. "Whether the contract is one of insurance or of indemnity," said one court, "there must be a risk of loss to which one party may be subjected by contingent or future events and an assumption of it by legally binding arrangement by another. Even the most loosely stated conceptions of insurance and indemnity require these elements. Hazard is essential and equally so a shifting of its incidence. If there is not risk, or there being one it is not shifted to another or others, there can be neither insurance nor indemnity. Insurance also, by the better view, involves distribution of the risk, but distribution without assumption hardly can be held to be insurance." (*Jordan v. Group Health Ass'n.*, 107 Fed. 2d 239, 245; see also: *Fageol T. & C. Co. v. Pacific Indemnity Co.*, 18 Cal. 2d 731; *Gregg v. Comm'r. of Corp. & Tax.* (Mass.), 54 N.E. 2d 169; *Comm'r. Banking & Ins. v. Community Health Service (N.J.)* 30 Atl. 2d 44; *Stern v. Rosenthal*, 128 N. Y. Spp. 711; *State v. Universal Service Agency (Wash.)*, 151 Pac. 768; 53 Yale L. J. 172; 23 Corn. L. Q. 188, 193; 119 A.L.R. 1241; 100 A.L.R. 1449; 63 A.L.R. 711; *Vance, Insurance*, 2d ed., p. 57.) Although some authorities have held that to constitute insurance the so-called insured must be indemnified by the payment of money (*Jordan v. Group Health*, *supra*, p. 245, note No. 13; *Moresh v. O'Regan (N. J.)*, 187 Atl. 619; 5 *Elliott, Contracts*, sec. 4020), or that statutes regulating insurance were intended to apply only to concerns

<sup>1</sup>"Sec. 593a (Health service corporations: Prerequisites to commencement of business: Supervision.) A nonprofit corporation may be formed under this article for the purpose of defraying or assuming the cost of professional services of licensees under any chapter of Division 2 of the Business and Professions Code or of rendering any such services but it may not engage directly or indirectly in the performance of the corporate purposes or objects unless:

"(1) At least one-fourth of all licensees of the particular profession become members;

"(2) Membership in the corporation and an opportunity to render professional services upon a uniform basis is available to all licensed members of the particular profession;

"(3) Voting by proxy and cumulative voting are prohibited; and

"(4) A certificate has been issued to the corporation by the particular professional board, whose licensees have become members, finding compliance with the foregoing requirements.

"Any such nonprofit corporation shall be subject to supervision by the particular professional board under which its members are licensed and shall also be subject to the provisions of Section 605c of this code. This section, except as expressly permitted herein, does not authorize the formation of any corporation for the purpose of rendering the professional services regulated by Division 2 of the Business and Professions Code. (Added by Stats. 1941, ch. 623, sec. 1.)"

organized for profit and not to charitable or nonprofit associations (Hall D'Ath v. British Provident Assoc. (1932), 48 Times L. R. 240; State v. Taylor (N. J.), 27 Atl. 797), there are more substantial reasons upon which to base a determination as to the status of the California organization.

The business of the Service lacks one essential element necessary to bring it within the scope of the insurance laws, for clearly it assumes no risk. Under the provisions of the contracts or group agreements, it is a mere agent or distributor of funds. It does not promise the beneficiary members that it will provide medical care; on the contrary, "the services which are offered to . . . beneficiary members of C.P.S. are offered personally to said members by the professional members of C.P.S. . . ." (See: Jordan v. Group Health Assn., *supra*, p. 246; Phez Co. v. Salem Fruit Union (Ore.) 201 Pac. 222.) The professional member is compensated for his services solely from the fund created by the monthly dues to the beneficiary members. Payments from the fund are made to the physician pro-rata in accordance with an established schedule. Under that plan, the amount of compensation of the professional members is variable and may be high or low, depending upon the incidence of sickness and the number of beneficiary members paying dues. Stated in terms of insurance, all risk is assumed by the physicians, not by the corporation, hence the only effect of requiring compliance with regulatory statutes would be to compel the acquisition of reserves contrary to the established method of operation. (See: Jordan v. Group Health Assn., *supra*, p. 251.)

This distinction has been recognized and applied by other courts which have considered the same question. In Jordan v. Group Health Assn., *supra*, the organization which distributed funds for medical care sought a declaration of its statute under the laws of the District of Columbia which define insurance in substantially the same terms as the California statutes. The corporate purpose of the association and its method of doing business was similar to that of California Physicians' Service. The court held that the corporation had assumed no risk. This conclusion applies more exactly to the California organization because of the total lack of a promise by the corporation to the beneficiary members to render any medical care. Except for the limited hospitalization obtainable by rural members in connection with the Farm Security Administration contract, the Service does not even promise to "use its best efforts to procure the needed services" as the District of Columbia corporation agreed to do, and does not obligate itself to pay the physicians a certain sum per month. The California physicians look solely to the monthly dues of the beneficiary members for compensation.

The case of State v. Universal Service Agency (Wash.), 151 Pac. 768, relied upon in the Jordan case, *supra*, p. 249, was an action by the insurance commissioner to forfeit the corporate franchise of the organization upon the ground that it was "doing an insurance business without complying with the statutes regulating the doing of such business." The applicable definition of insurance was similar to, if not identical with, that of this state, and the method of doing business was the same as that of the California Physicians' Service, including the type of contract used. And again the want of assumption of any hazard or risk was the basis for holding that the corporation was not engaged in the insurance business.

In the case of Commissioner of Banking and Insurance v. Community Health Service, Inc., 129 N.J.L. 427, 30 Atl. 2d 44, the insurance commissioner sued the defendant corporation to recover a statutory penalty for conducting an unlicensed insurance business. The corpora-

tion had made contracts with licensed physicians under which they agreed to render professional services for a certain stipulated compensation to those members of the general public who paid the corporation a specified sum each month. The physicians' services were engaged by the corporation for a period of one year, and from year to year thereafter, for a fixed consideration which varied with the number of contract holders but not with the amount of service rendered by the physician to any or all of the contract holders. The court, relying upon State v. Universal Service Agency, *supra*, and Stern v. Rosenthal, 128 N.Y.S. 711, held that the corporation was not engaged in the business of insurance because, as between the corporation and the physician, nor between the physician and the subscriber, was the compensation or any other element of the arrangement between them affected by any contingency, hazard or risk which the corporation assumed and insured against. (See also: Vrendenburgh v. Physicians Defense Co., 126 Ill. App. 509; State v. Laylin, 73 Ohio St. 90; 53 Yale L. J. 172.)

In both the Jordan case, *supra*, and in State v. Universal Service Agency, *supra*, as is true in the present case, reliance was placed upon Physicians' Defense Co. v. O'Brien, 100 Minn. 490, Physicians' Defense Co. v. Cooper, 199 Fed. 2d 576, and State v. Globe Casket Co., 82 Wash. 124. The Physicians' Defense cases involved contracts to supply legal service to physicians in malpractice suits; the latter one concerned an agreement for burial expense. But in each of those cases there was a contract providing indemnity against a hazard which might cause loss to the corporation and, for that reason, the decisions are not herein point.

There is another and more compelling reason for holding that the Service is not engaged in the insurance business. Absence or presence of assumption of risk or peril is not the sole test to be applied in determining its status. The question, more broadly, is whether, looking at the plan of operation as a whole, "service" rather than "indemnity" is its principal object and purpose. (Jordan v. Group Health Assn., *supra*, pp. 247 et seq.; see: Vrendenburgh v. Physicians' Defense Co., *supra*, p. 513; State v. Laylin, *supra*, p. 98; Commonwealth v. Provident Bicycle Ass'n., 178 Pa. 636, 642; Sisters of Third Order of St. Francis v. Gillaume, 222 Ill. App. 543; 3 Univ. of Pittsburgh L. Rev. 250; 52 Harv. L. R. 814, 815; 23 Corn. L.Q. 188; 29 Mich. L. Rev. 378; Vance, Insurance, p. 61.) Certainly the objects and purposes of the corporation organized and maintained by the California physicians have a wide scope in the field of social service. Probably there is no more impelling need than that of adequate medical care on a voluntary low-cost basis for persons of small income. The medical profession unitedly is endeavoring to meet that need. Unquestionably this is "service" of a high order and not "indemnity."

The fact that the Rural Health Service Agreement provides for limited hospitalization does not make the business of the Service that of insurance. So far as the record shows, a participating hospital must look only to the pooled fund of the Service for payment for facilities furnished to a beneficiary member. Also, the additional features of hospitalization and reimbursement for drugs are not distinguishable from other medical care obtainable on the group basis, and they are merely incidental to the plan or scheme as a whole. (See: Jordan v. Group Health Assn., *supra*, p. 244 note No. 10.)

Furthermore, the legislature by the enactment of section 593a of the Civil Code, with its express provision for limited regulation of nonprofit organization of a professional character by the attorney general and the particular professional board, necessarily intended that such organization should be exempt from regulation by the insurance commissioner. (See: 52 Harv. L. Rev. 816; 53



Yale L. J. 171 et seq.) One of the reasons behind the declaration of the earlier cases that it was against public policy for a corporation to engage in the practice of medicine was because the control of its activities was placed in the hands of laymen. (See: *Pacific Employers Ins. Co. v. Carpenter*, *supra*; *Painless Parker v. Board of Dental Exam.*, 216 Cal. 285, 296; 52 Harv. L. R. 811; 53 Yale L. J. 170.) To allow the insurance commissioner to impose the extensive regulations provided for in the Insurance Code upon the activities of the Service would result in the same evil. (See: Yale L. J. 171.) Since section 593a of the Civil Code is applicable to the organization whose status is here under attack, it must be presumed that the legislature weighed this evil against possible exploitation of the public and concluded that the limited regulation provided by the new statute was sufficient. Also, it may be noted, section 433.6 of the Political Code dealing with payroll deductions for state employees who join any group medical plan, makes a clear distinction between regular insurance companies and "non-profit membership corporations organized under the laws of this State, for the purpose of defraying the cost of medical services. . . ." (See also: Stats. 1939, ch. 250 p. 1505; Stats. 1940, First Extra Session, ch. 45, sec. 6.7.)

This conclusion becomes more apparent when the purpose and nature of many of the legislative requirements are considered, particularly those relating to the maintenance of reserves and to the regulation of investments and financial operations. The extensive insurance regulations primarily are designed to protect the insured or the public, from the insurer. (52 Harv. L. Rev. 815.) Such regulations become important only if the insurer has assumed definite obligations; conversely, it is evident that they are not intended to apply where no risk is assumed and no default can exist. Furthermore, by the very nature of its operations, the Service could not accumulate vast reserves. The flow of funds from patient to physician primarily is on a monthly basis of pay-as-you-go and to require reserves would be a useless and uneconomic waste. (*Jordan v. Group Health Ass'n.*, *supra*, p. 251; see: 53 Yale L. J. 171.)

For these reasons the respondent is not engaged in the business of insurance within the meaning of the regulatory statutes but is subject to the limited supervision provided by sec. 593a of the Civil Code. The judgment of the trial court in this regard is not too broad, for every decision is limited to the evidence upon which it is based.

EDMONDS, J.

WE CONCUR:

Shenk, J.  
Ward, J. Pro. Tem.  
Carter, J.  
Peters, J. Pro. Tem.

I CONCUR IN THE JUDGMENT: Schauer, J.

CONCURRING OPINION

Gibson, C. J.

## CONCURRING OPINION

I concur in the judgment solely on the ground that the Legislature, by the enactment of section 593a of the Civil Code, exempted organizations coming within its scope from regulation by the Insurance Commissioner. By providing for supervision by a professional board and by the attorney general (Civ. Code. secs. 593a, 605c), the Legislature has evidenced an intention to free such organizations from other regulation and from the necessity of complying with the various requirements, such as the maintenance of reserves, which are imposed on regular insurance companies. The need for regulation or supervision, the amount thereof and the persons, bodies or officers who should supervise or regulate are all matters which are confided to the Legislature, and it was within the legislative discretion to provide that a limited regulation of such nonprofit organizations was sufficient.

I cannot, however, concur in that portion of the opinion declaring that the plaintiff is exempted from regulation by the Insurance Commissioner because it is not engaged in the business of transacting insurance, but is merely agreeing to render service. The true test is not the character of the consideration agreed to be furnished, but whether or not the contract is aleatory in nature. A contract still partakes of the nature of insurance, whether the consideration agreed to be furnished is money property or services, if the agreement is aleatory in nature and the duty to furnish such consideration is dependent upon chance or the happening of some fortuitous event. (See Rest., Contracts, sec. 291.) In the present case the agreement is to make payments to member doctors for medical services to the beneficial members and the duty to make such payments is obviously dependent upon chance or the happening of a fortuitous event, since the necessity for the services, and also for the agreed payment, is dependent upon the members' sickness or accidental injury.

GIBSON, C. J.

## Clinical Laboratory Technicians Must Be Licensed

Because of repeated indications that "a number of physicians throughout California are not conversant with provisions of the Clinical Laboratory Act" relative to employment of clinical laboratory technicians, W. L. Halverson, M.D., Director of Public Health, has asked CALIFORNIA MEDICINE to call attention to some of the salients.

"This law," Dr. Halverson says in a letter to the editor, "requires that any technicians who engage in clinical laboratory work shall be in possession of a license issued by the California State Department of Public Health. Violation of the Act, either on the part of the technician or of the employer, is a misdemeanor."

The letter continues: "While physicians may legally operate clinical laboratories under their license as physician and surgeon, this does not exempt them from the provision of the law requiring the employment of licensed technicians to actually do the work in the laboratory. It

has been our observation that many physicians are not cognizant of this requirement. While the law does permit one apprentice to work in a laboratory, this is with the proviso that such apprentice be under the direct supervision of licensed personnel.

"It should also be noted that any physician who assumes the responsibility for directorship of a laboratory must actually spend sufficient time in the laboratory to supervise adequately the work of the personnel. Under the provisions of the law, supervision cannot be delegated to a technician on the staff who holds only a clinical laboratory technician's license.

"Detailed information concerning the provisions of the law may be secured by physicians from the Division of Laboratories, 3023 Life Sciences Building, Berkeley 4. Copies of the law and the regulations adopted under the law will be sent upon request."



# Letters to the Editor . . .

## CONTRADICTORY TERMINOLOGY IN OBSTETRICS

The growth in knowledge of developmental anatomy during this century has outdistanced the development of a rational terminology. Consequently, much of the terminology of developmental anatomy and obstetrics is confusing or contradictory. While an adequate outline of the semantic deficiencies of morphogenesis cannot be attempted here, let us look at some of the more flagrant examples of faulty terminology for which revision is not difficult.

The terms *ovum*, *embryo* and *foetus* are used more or less indiscriminately to designate the product of conception. This use probably stems from His' division of human gestation into three periods: the ovular, the first two weeks; the embryonal, the third to fifth week; and the fetal, the sixth week to term. Later authors have reserved the word *foetus* for the child *in utero* after the third month of gestation. There exists no morphologic nor physiologic basis for these and similar arbitrary divisions of the span of gestation. Here we find the same term used to describe the unfertilized female gamete and the two-week-old product of conception. The advantages of a word describing the total product of conception from the two-cell-stage to term are apparent; and for this purpose the convenient term of *conceptus* has much to recommend it. The word *ovum* would then be limited to the unfertilized female gamete and the word *zygote* would then be reserved for a fertilized or parthenogenetically activated gamete in the process of the first cleavage stage.

*Foetus* has also been defined as "the medical synonym for embryo" (J. Needham, "Biochemistry and Morphogenesis," p. 684) and this definition has met with some acceptance. Indeed, there exist no criteria by which the two words may be distinguished. But the *conceptus* comprises more than the embryo or foetus. In 1889 Hubrecht discovered the trophoblast and this introduced an additional complexity into the accepted meaning of the word *embryo*. Orr terminological inadequacy is now such that it is not uncommon to find an author defining *trophoblast* as "the non-embryonic part of the mammalian blastocyst . . . which later develops into the foetal portion of the placenta" and then defining *fetus* as "the medical synonym for embryo" (ibid, pp. 684, 688). It would contribute much to the clarification of the subject of morphogenesis if the word *embryo* were limited to those anlagen of the *conceptus* that enter directly into the formation of the post-natal individual.

Separating the definitive *embryo* from the *conceptus*, we are left with such *extra-embryonic* structures as the amnion, allantois, yolk-sac and umbilical cord. Although these structures are closely associated in development with the definitive embryo, they are properly called *extra-embryonic* since they comprise no part of the post-natal individual. The remaining trophoblast, composed of cellular and syncytial elements, is correctly described as the *non-embryonic* portion of the *conceptus*, since the cleavage of the zygote results in the precocious segregation of the trophoblast cells from the remaining cells of the early *conceptus*; and from this time on the two cell types go their independent way and the one cannot form the

other nor be formed from the other. The dichotomy between trophoblast and the non-trophoblastic elements of the *conceptus* was dramatically demonstrated by Maximov when he cultured entire rabbit *conceptuses in vitro* and found that the definitive embryo and extra-embryonic membranes were, after a fortnight, completely destroyed by the infiltration and erosion of the trophoblast which consumed all non-trophoblastic elements in the culture (A. Maximov, *Carnegie Contrib. Embryol.*, 16:47, 1924). In terms of the older terminology one would perhaps describe this case as one in which the "embryo" consumed itself.

The misuse of the word *embryo* has been responsible for such errors, perpetrated in reputable textbooks, as describing the trophoblast as ectodermal when it is, in fact, autonomous in origin and fate of the three primary germ layers of the remainder of the *conceptus*. In the case of tubal pregnancies in which the trophoblast destroys the definitive embryo with the formation of a so-called "blood mole" the value of an adequate terminology for descriptive purposes is clear. (The latter phenomenon might be considered the *in vivo* counterpart of what Maximov described as occurring *in vitro*). The same generalizations apply to the overgrowth of trophoblast in hydatid mole and chorionepithelioma—which occur in the absence of the definitive embryo. And surely the case of identical twins or triplets, etc., sharing a single trophoblastic blastocyst (or chorion) strikingly demonstrates the need for the use of the proper terms to distinguish such a monozygotic *conceptus* of a fixed genetic constitution from the definitive embryos which in part comprise that *conceptus*.

Indeed, the use of the word *embryology* to describe the total phenomenon of gestation is not altogether adequate, and the growing use of such alternative terms as *developmental anatomy* or *morphogenesis* is a hopeful sign.

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## IRON SALTS VS. PLUMBISM

The influence of iron salts on the development of lead poisoning has been studied by Heppel<sup>1</sup> and his associates of the National Institute of Health, Bethesda, Maryland.

Albino rats were fed experimental diets from the time of weaning. The animals were weighed at four to seven day intervals, and tail blood used for smears and micro-determinations. In a typical experiment, the average weight of ten young rats reared on a non-toxic basal diet was 43.2 g. at the time of weaning. The weight increased to an average of 239.4 g. by the end of 65 days. The average hemoglobin content increased to 16.1 g. per 100 cc. of blood and the average hematocrit reading to 49 per cent in the same period of time. Terminal blood smears showed an average of 3.8 polychromatic red cells per 1,000 r.b.c. In a parallel test of ten weanling rats fed a lead diet (0.09 g. lead per 100 g. of basal diet) the

average weight increased to only 143.2 g., the hemoglobin fell to 10.5 g. per 100 cc., and the hematocrit reading to 39 per cent by the end of 65 days. Terminal blood smears showed a 12-fold increase in polychromatic red cells (49 per 1000 r.b.c.) In a third group of weanling rats, in which 1.13 g. ferric citrate per 100 g. was added to the lead diet, the average terminal weight was 203.1 g.; hemoglobin 14.7, hematocrit reading, 51 per cent and polychromatic count only slightly above normal (8.2 per 1000 r.b.c.).

Given in this concentration, ferric citrate thus almost completely prevented the toxic effects of the lead diet. Since control tests with sodium citrate did not inhibit toxicity, the conclusion was drawn that the prophylactic effect was not due to the citrate radicle.

The mechanism of his antitoxic action of iron salts has not yet been determined. A possible explanation would be the assumption that iron citrate interferes with the gastrointestinal absorption of lead. Such a possibility was suggested 15 years ago by Miyasaki.<sup>2</sup> Confirming this theory, analyses have shown a much lower lead content of tissues of rats whose lead diet contained supplements of iron citrate. Studies of the absorption of radioactive lead in the presence and absence of iron compounds are now in progress.

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#### ANTI-ALLERGIC "BLOCKADE"

In the course of studies of experimental drug allergy, Chase<sup>1</sup> of the Rockefeller Institute noted that sensitization was at times unsuccessful in guinea pigs which previously had ingested or had otherwise been treated with the same drug. Experiments were therefore undertaken to establish at will such an anti-allergic refractory state.

For his first experiments 2:4 dinitrochlorobenzene was chosen as the sensitizing agent. This is a well known active dermal allergenic agent for man. A 1 per cent solution of this drug in olive oil was fed to guinea pigs in 0.3 cc. doses. The doses were given in such a way as

to avoid contact with the muzzle of the animal. The feedings were made daily for six days, followed by an eight-day rest period, two to three such courses being given. Control feedings were made with the vehicle alone (olive oil).

After a rest period of two weeks the animals were subjected to active sensitizing. This consisted of six or more intracutaneous injections of the drug over a period of several weeks. Two weeks after the final sensitizing dose, a test of acquired dermal sensitization was made by painting the skin with a dilution of the incitant in olive oil. Of 77 control animals, none escaped sensitization, 90 per cent of them showing maximal or near-maximal skin reactions. Of 93 animals given a prior feeding with the drug, 67 per cent escaped all but a trace of sensitization. Only 3 per cent of them gave maximal skin reactions. There was thus a well-nigh complete inhibition of subsequent dermal sensitization as a result of previous feeding with the allergenic drug.

To test the duration of this refractory state, groups of animals were fed the same drug and at varying intervals after the final feeding were given the routine dermal sensitizing course. The refractory state was still apparent even when the interval between the final feeding and attempted sensitization was as long as 27 weeks. Longer intervals were not tested.

The refractory state is apparently specific. Animals fed 2:4 dinitrochlorobenzene are fully susceptible to subsequent dermal sensitization with o-chlorobenzoyl chloride. Specific feeding, however, is ineffective therapeutically. Courses of feeding given to animals previously sensitized to 2:4 dinitrochlorobenzene caused no appreciable reduction in the degree of dermal hypersensitivity. This is contrary to the findings of Park<sup>2</sup> and Stevens<sup>3</sup> who have reported a partial desensitization of sensitive human beings by ingestion of specific allergens.

No theory is as yet suggested to account for Chase's pe-allergic "blockade." Serum titers have not yet been reported. It is evident, however, that prophylactic anti-allergic "blockade" is of suggestive clinical interest.

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## BOOK REVIEWS

**DISEASES OF THE ADRENALS.** By Louis J. Soffer, M.D., Adjunct Attending Physician, The Mount Sinai Hospital, New York City. Cloth. Pp. 304, illustrated with 42 engravings and 2 colored plates. Philadelphia: Lea & Febiger, 1946.

As is so frequently noted in recent days, the science of endocrinology is growing up. No longer are monographs on this subject composed largely of bizarre photographs and equally bizarre clinical guesswork. Modern endocrinology speaks in terms of fundamental physiology and deals with an ever increasing number of specific chemical entities of known structure and function.

This little book by Dr. Soffer on *Diseases of the Adrenals* is a good example of the modern approach. While in clinical practice specific adrenal disease is relatively rare, it behooves every practitioner, internist and surgeon to have a working knowledge of adrenal function, especially those functions relating to the electrolytes, specifically sodium and potassium; to carbohydrate and protein metabolism; and to sexual development and function.

The chapters on physiology are clear and concise. Existing lacks in knowledge are frankly stated and there is a refreshing lack of speculative dogmatism.

The clinical discussions of Addison's disease, the adreno-genital syndrome, and the various adrenal tumors are excellent and not too long. They are well illustrated with selected case histories. The latter are condensed to their essentials. The clinical manifestations are well correlated with known physiology, and the sections on specific therapy are definite and inclusive.

The style is simple and easy to read.

The bibliography is most comprehensive, the section on physiology alone citing 219 references.

The reviewer enjoyed this book and recommends it for general as well as more specific reading.

**DISEASES OF THE RETINA.** By Herman Elwyn, M.D., Senior Assistant Surgeon, New York Eye and Ear Infirmary. Cloth. Price, \$10.00. Pp. 587 with 170 illustrations, 19 in color. Philadelphia: The Blakiston Company, 1946.

The author has divided the subject matter into eight parts and forty-two chapters. The first two parts include 17 chapters dealing with diseases of the retina resulting from disturbances in circulation and from vascular malformations. This is covered in a way which makes interesting reading, and it is well illustrated with fundus photographs and reproductions of many pathologic sections. An attempt is made in these chapters to correlate the fundus picture with the underlying systemic vascular disease or anomaly so that it makes a handy reference volume for both the ophthalmologist and internist. Arteriosclerosis, both general and local, in the eye-grounds, essential hypertension and arteriospastic retinitis in kidney diseases, is taken up in considerable detail. The paragraphs on pathologic anatomy and pathogenesis in each chapter are short and to the point.

In the chapter on diabetic retinitis, an interesting comparison is drawn between diabetes, essential hypertension and chronic simple glaucoma. It appears to be the author's belief that in all these diseases the mechanisms for control of normal values of blood sugar, blood pressure and intra-ocular pressure, respectively, are inherently deficient. He attributes this inherent instability to an in-

herited defect present in the germ plasm and says that it appears at a definite early period in life. He states that in the case of diabetes, the cause of the instability is not to be found in the effector organs such as the liver, in the islands of Langerhans or in the peripheral vegetative nervous system. He stresses the central nervous system of brain as the regulating mechanism.

The remaining chapters include many of the rarer diseases of the retina of the degenerative type, such as retinitis pigmentosa, heredo-degeneration of the macula, amaurotic family idiocy, etc.

Inflammatory disease of the retina discussed include tuberculosis and syphilis. There is a short chapter each on retinal changes in septicemia and in subacute bacterial endocarditis. Only one case was reported to prove that tuberculosis of the retina could exist in pure form.

In the section under tumors of the retina, glioma or retinoblastoma is discussed extensively. The technique of radiation therapy as outlined by Martin and Reese is given under the paragraph for treatment. The rarity of other primary tumors of the retina is emphasized. He states that there are only three reports in the literature, one of a perithelioma of the retinal vessels, one of endothelioma of the nerve head, and one of sarcoma of the retina.

Approximately sixty pages are given to a discussion of the diseases leading to retinal detachment and to the etiology clinical picture, pathologic anatomy and treatment of the condition. For the benefit of the few medical men and possibly the rare ophthalmologist inclined to write off one eye with retinal detachment without attempting surgery, figures are given on bilaterality of the condition. The figure approaches 18 per cent in one large series.

**ANESTHESIA IN GENERAL PRACTICE.** By S. C. Cullen, M.D., Head of Division of Anesthesiology, Department of Surgery, State University of Iowa's Hospitals; Associate Professor of Surgery (Anesthesiology), State University of Iowa's College of Medicine. The Year Book Publishers, Inc., Chicago. Price, \$3.50.

The chapters of this book on Preanesthetic Medication; Airway Inhalation Anesthesia Agents and Techniques; Signs of Anesthesia; Choice of Anesthetic Agent and Technique; Recognition and Treatment of Shock; Oxygen Therapy; Pre and Postoperative Care of the Patient and Explosion Hazards are presented in a clear, concise manner. They should be of value to beginners in anesthesia and to those doing anesthesia on a part-time basis.

The chapters on Spinal Analgesia and Regional are not on a par with the remainder of the book and contain statements such as: "The selection of a drug for spinal analgesia can be made solely on a time basis. Toxic properties of these drugs need not be considered because toxic reactions do not occur following the introduction of these drugs intrathecally." Such statements interpreted literally by a novice could easily lead to a fatality from administration of too large a dose of a toxic anesthetic agent.

The description and illustrations of the correct treatment of reactions to local anesthetic agents are well done.

On the whole the book is well written and contains much of value.

**HUMAN EMBRYOLOGY.** By Bradley M. Patten, Professor of Anatomy in the University of Michigan Medical School. Cloth. Price, \$7.00. Pp. 776 with 1366 drawings and photographs grouped as 446 illustrations; 53 in color. Philadelphia: The Blakiston Company, 1946.

This book perhaps will not be considered a classic work in the field of human embryology because of the necessary limitations imposed upon it as a textbook primarily for the medical student, but as such a text it cannot be excelled.

The fluent literary style, the adequate illustrations, the good printing and excellent paper all go together to make a fine book. The beginning medical student will find it easy to study; the practitioner will find it difficult to put down once he opens its pages. There are many clinically important subjects discussed, and to the doctor who is a student, as well as a surgeon, the sections of the book dedicated to the abnormalities of development of the various systems will be most valuable in the interpretation of many pathological conditions.

The bibliography is excellent and contains numerous references to work of clinical importance. This enhances further the value to the clinician who might wish more detailed information on a special subject.

**THE CARE OF THE AGED (GERIATRICS).** By Malford W. Thewlis. Fifth edition. (St. Louis. The C. V. Mosby Co., 1946.) 500 pages. Price, \$8.00.

Though Thewlis emphasizes the present need for increased, active interest in the growing population of patients past 60, his book is not merely an expression of the current enthusiasm toward geriatrics as a medical specialty. The first edition of the text was published in 1919. In his preface to the third edition, the author stated: "There is a wider recognition today that the ills of the aged are a special problem: first, because many of them are peculiar to the aged, and second, because the presence even of those which also occur in younger people raise special therapeutic problems in senescence." Having suggested by simple prefatory statement that the care of the elderly may become a specialty, he has done with propaganda and proselyting and settles to his text.

The volume is written in eight parts and thirty-three chapters. The first 121 pages are essentially concerned with the general problems of uneventfully growing old. Here is clearly, sensibly, and forcefully expressed the art of treatment of the aged—the philosophy of "geratology" and its relation to the aged group and aged individual. Separate attention is given to the neglect of the elderly, stress and longevity, medico-legal relations most apt to involve the group and its physicians, the general and differential use of therapeutic agents, the details of nursing care. Anatomic, physiologic, and pathologic alterations of senescence are adequately described without the clutter of minutiae. A separate chapter stresses the need for vigilance toward pre-symptomatic disease in routine examinations. In the chapter devoted to hobbies, the author not only stresses their importance but provides several pages of practical suggestions for such activities.

Thewlis writes: "Geriatrics is based upon three fundamental principles: (1) that senescence is a physiologic entity like childhood and not a pathologic state of maturity; (2) that disease in senescence in a normally degenerating organ or tissue is not a disease such as is found in maturity, but is complicated by degeneration; (3) that the object of treatment in senescence should be to restore the diseased organ or tissue to the state normal to senescence and not a restoration to the condition normal in maturity." In the main body of the text which is devoted to Disease of Metabolism and Endocrine Disorders, Infectious Diseases and Focal Infection, and

Systemic Pathologic Conditions, these principles are repeatedly stressed. In this sense these chapters remain throughout devoted to the consideration of aged patients.

In general it is obviously better for the reader to consult the literature and texts devoted to the consideration of the particular disease or system involved by disease in studying an illness concerning a patient of any age group. Statements throughout the text—as some in the chapter on the Cardiovascular System, to be particular—are misleading if one relies solely upon Thewlis' discussions. This is a valid criticism of all geriatrics texts: what they have to tell us that is peculiar to the aged does not supplant that which is peculiar to the disease. However, it is in this special regard that Thewlis' book surpasses its chief rival in the field—Stieglitz's "Geriatric Medicine. . . ." Thewlis seems in general aware that his material does not supplant but only supplements. Furthermore, though other authors have contributed to "The Care of the Aged," their chapters are brief, and the effect is of single authorship. This, or careful editing, has prevented the striking unevenness of merit and bothersome repetition that depreciate Stieglitz's book.

"The Care of the Aged" is practical. It contains all presently available material that is pertinent to its thesis. It is clear, readable and well organized. The index is detailed, extensive, and accurate. Discussions include the scientific finesse of anesthesia, the mathematical angle in surgical risk, the proper size of sox and weight of underwear, the normalities as well as the abnormalities of geriatric sex life, when to take a bath, and how best to clean false teeth.

Throughout there is suggested the thought expressed in a chapter summary: "Let the ultimate comfort of the patient be the main consideration. Be gentle, be conservative, be careful and be kind."

**WOMEN IN INDUSTRY.** By Anna M. Baetjer, SC.D., Asst. Professor of Physiological Hygiene, School of Hygiene and Public Health, The Johns Hopkins University. W. B. Saunders Company, Philadelphia and London—1946. Price, \$4.00.

A cursory inspection of this book would lend belief that it is of value only to the industrial physician, personnel director, or job placement officer. Yet further study reveals its importance to the profession at large.

It has been estimated that 16 million women will be employed in industry by 1950, barring serious economic disorders. The problems entailed cannot be met by industrial medicine since a majority of these women will be working in small plants where there is no medical supervision. The responsibility, therefore, must be met by the general practitioner and special aspects of it by the gynecologist and obstetrician. Too long has the profession been ignorant of what women can or cannot do; doctors have permitted women to do certain tasks when they should have been refused, or have denied them privilege when they should have been allowed. These errors have been based upon legendary assumptions. Dr. Baetjer dispenses these false notions by statistical evidence.

The book deals with the anatomy of the female as to height, weight, reach, fatigability, susceptibility to certain types of strain (or non-susceptibility), types of work to which women are peculiarly suited, value of rest, especially as to change of routine. It considers the incidence of absenteeism, accidental injuries, occupational diseases among women, and such special problems as pregnancy, lactation, menses, menopause, fertility, and the like. An appendix contains a summary of the state labor laws for women of the various states.

"Women in Industry" is not a clinical study, but Dr. Baetjer has contributed a valuable group of statistics



which should form a basis for sane handling of women who choose to work.

**PULMONARY TUBERCULOSIS IN THE ADULT, ITS FUNDAMENTAL ASPECTS.** By Max Pinner, M.D. Chas. C. Thomas, publisher, Springfield, Ill. 1945. XIII and 579 pages. Fifty-nine figures and 4 graphs. \$7.50.

This clear, coherent and comprehensive exposition of the fundamental mechanisms underlying clinical tuberculosis should be a valuable guide, not only to the general practitioner and the medical student but even to those who have long specialized in this tangled field.

The slow multiplication, high resistance and exacting nutritive requirements of the tubercle bacillus underlie its clinical behavior and suggest means of controlling it. Pathological, radiological and clinical findings contribute to the understanding of the histogenesis of tuberculous lesions, as exemplified by the classification of cavities and their prognostic and therapeutic implications.

Protective tissue reactions, strict localization of lesions, and acute inflammatory response at the site of implantation characterize both native and acquired resistance to tuberculosis. Humoral antibodies are irrelevant in this disease. Skin and general tissue hypersensitivity must be distinguished, and the protective value of vaccination with BCG balanced against its practical disadvantages.

The various lesions which develop following reinfection differ in their morphology, mode of origin and later course. Nutritional, endocrine, constitutional, meteorological and other factors may influence their evolution.

The practical utility of the National Tuberculosis Association Classification of Pulmonary Tuberculosis is conceded but Ranke's stimulating hypothesis has more imaginative appeal. Pulmonary phthisis, with localization in one organ system, acute episodes of exudation and tissue destruction with slow chronic reparative processes or the dangerously defensive phenomenon of excavation reflect the immunobiological constellation of the host and the tubercle bacillus and the special structure and function of the lung. Exudation, caseation, fibrosis and cavitation are interpreted from this point of view.

Case finding with the demonstration of tuberculous infection by skin tests, of pulmonary foci by the x-ray, and of the specific nature of the lesion by bacteriological findings, and the clinical roentgenological and laboratory evaluation of the activity of the process illustrate the value of the combined approach. The reliance of negative sputum findings in tuberculosis, the dismissal of quantitative bacteriological findings, the skeptical rejection of all hematologic and serological aids in prognosis and the advocacy of clinical experimentation without preliminary animal studies may be questioned by other workers.

Factors involved in the healing of tuberculous lesions include local rest, elastic relaxation, bronchial occlusion, decreased tidal air, blood and lymphatic flow, and oxygen availability, and increased fibrosis. The treatment of tuberculosis by simple rest and medical measures is emphasized.

The discussion of collapse therapy is based on the assumption that healing by rest alone, if it can be achieved, is preferable to healing under collapse. Little value is attributed to phrenic interruption, pneumoperitoneum and other minor collapse measures.

An epidemic curve in tuberculosis, with a tendency of the disease to diminish in countries in which it has been established, is accepted despite glaring exceptions and alternative explanations.

The annotated references which occupy more than a quarter of the book not only cite the substance of each contribution, but often include a critical evaluation of its significance and suggestions of implications or other pertinent data. Photographs of gross and histological preparations and single or serial roentgenograms graphically illustrate many of the points made in the text.

Although some may differ with the author on individual conclusions, it must be admitted that he is unsurpassed in his command of the literature in this field and is admirably fitted for its evaluation. It is gratifying in these hurried and mechanized days to find such a product of deliberate contemplation and analysis of fundamental concepts as applied to what is still the most important single disease afflicting man.

#### SUBSTANCES PLACED ON BODY SURFACE NEED MORE STUDY, JOURNAL SAYS

Referring to cases of poisoning associated with the use of thioglycolic acid in the so-called cold wave process for permanent waving of the hair, the June 29 issue of *The Journal of the American Medical Association* says editorially that "as much careful evidence needs to be accumulated regarding the safety of substances placed on the surface of the body as those taken into its interior before these processes are released for use to the general public."

The statement was made in connection with an article in which Carey P. McCord, M.D., of Detroit, called attention to certain facts which he believed were overlooked by Lawrence H. Cotter, M.D., of New York, in his discussion of the cold wave process in *The Journal* of June 15. Dr. McCord believes that damage to the liver by the use of cold wave chemicals has not yet been defi-

nitely shown in any instance and that allergic responses are infrequent when materials used are properly prepared.

"Notwithstanding these statements," the latest issue of *The Journal* says, "the fact remains that some 50 different commercial agencies are engaged in the manufacture of materials used in cold wave processes, that there exist no definite standards as to what is safe or harmful, that experimentation before launching such products is for the most part inadequate and incomplete and that it is time for public recognition of the fact that as much careful evidence needs to be accumulated regarding the safety of substances placed on the surface of the body as those taken into its interior before these preparations are released for use to the general public."



## MEDICAL JURISPRUDENCE

### MALPRACTICE: SUFFICIENCY OF EVIDENCE: DEGREE OF SKILL REQUIRED OF A PHYSICIAN

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A recent case decided by the District Court of Appeal of the State of California again goes into a detailed consideration of the medical procedures and surgical techniques which were employed during an operation, in order to determine whether or not the operating surgeons had been negligent. The surgeons were absolved of any liability.

In this case the California Appellate Court was presented with the following situation: The patient, Mr. A, while constructing an addition to his home, was attempting to split lumber which was nailed together. In this process, he was using a carpenter's wrecking bar upon which he was hammering with a hammer, while holding the bar across his thighs. Suddenly, he felt something strike his right eye with a resultant severe burning pain, lasting for approximately one-half hour. He then looked into a mirror and observed a small red spot in the extreme right corner of his eye.

After consulting several hospitals and physicians, Mr. A went to defendant Dr. B's office and was taken to Dr. X's office in the same building and x-ray pictures were taken by the last named doctor. It was determined that an operation was necessary and Mr. A was taken to a hospital where the operation was performed. The operation was described by the defendant, Dr. B, as follows:

"After the eye was anaesthetized, the conjunctiva was picked up approximately over this foreign body and was dissected back over this foreign body, exposing this sclera—that is, that dense solid membrane, the sclera. Then a little opening was made in the wall of the eye with a cataract knife, just a tiny little opening, and then the magnet was put up against this opening and the current turned on. That was done at least a dozen times, and no foreign body came. And then after I saw that the magnet was not going to pull the foreign body, I took a tiny little pair of iris scissors. The incision was just as wide as that little knife. The cataract knife. Then after we could not get the foreign body with the magnet—it seemed to be non-magnetic, wouldn't come to the magnet—I introduced the tip end of a little pair of scissors about four millimeters—into approximately where this foreign body was, getting it close. I did that in preference to putting the tip of the magnet, because the magnet is a great big thing and would have enlarged the wound. I used the scissors, because the scissors are the best type of steel; and by putting the scissors into that little opening, almost in contact with the foreign body,

then putting up the magnet—touching the magnet on that, I could work in the small opening."

A few days after the operation Mr. A's eye was swollen shut and according to plaintiff, Dr. B looked into the plaintiff's eye without an instrument and said, "My God, something's happened! You have panophthalmitis." It was alleged by plaintiff that by reason of the negligence of the defendant doctors in the performance of the operation in question, there ensued an irritation of the tissues and an infection in the eyeball and eye, which resulted in an inflammation of the eyeball and eye, and panophthalmitis and iritis and other injuries, culminating in the total loss and destruction of the use and sight of the right eye and seriously endangering the plaintiff's left eye so that for several months the plaintiff was threatened with total blindness.

The plaintiff in this action did not present any expert testimony as to the diagnosis being incorrect nor as to what method or means in the exercise of ordinary care and skill, other than that used by the operating physicians, should have been employed.

In absolving the defendant physicians of any liability, the court followed the well-known rule on the subject of the care and skill required of physicians in the treatment of patients, stating that the law requires of the physician only that he shall have the degree of learning and skill ordinarily possessed by physicians of good standing, practicing in that locality, and that he shall exercise reasonable and ordinary care and diligence in treating the patient and in applying such learning and skill to the case. The court continued saying that "the law takes cognizance of human weakness and liability to err in the application of skill and learning, and it requires only the exercise of reasonable and ordinary care and diligence to avoid error."

The plaintiff based his action on the theory of negligent diagnosis and operative technique on the part of the defendant doctors, claiming there was error in locating the position of the foreign object and error in the determination that it was not magnetic. The court stated that a case of mistaken diagnosis does not render a physician liable, saying that "when due care, diligence, judgment and skill are exercised, a mere failure to diagnose correctly does not render a physician liable." The court concluded by saying that before the plaintiff can recover, he must show by expert testimony that the defendants failed to use the degree of care and skill ordinarily exercised by other surgeons in their locality.

